XII No. 7
1950

Journal of the

# AMERICAN PHARMACEUTICAL ASSOCIATION

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Practical Pharmacy Edition

# NEW RELIEF FOR THE ASTHMATIC

## *with Norisodrine® Powder and the Aerohalor®*

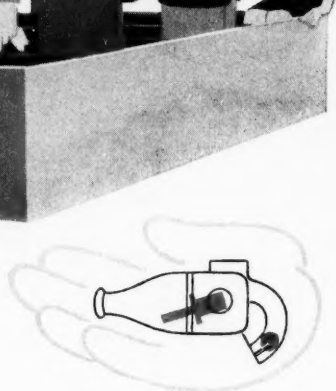
**KEEP YOUR EYES ON THIS PRODUCT!** Here's why: The conveniently carried Aerohalor has now been teamed with an effective bronchodilating powder to bring quick relief in bronchial asthma. The drug is NORISODRINE Sulfate powder (Isopropylarterenol Sulfate, Abbott)—supplied in multiple-dose Aerohalor* Cartridges.

The patient—suffering from either mild or severe asthma—simply inhales orally three or four times and the attack usually ends quickly. Clinical results show that NORISODRINE, a sympathomimetic amine, has restored and maintained activity for many chronic asthmatics.

Physicians and asthmatics have given a sincere welcome to the symptomatic relief so effectively and conveniently obtained with NORISODRINE powder. Abbott is now pushing this product with heavy promotion and detailing. Are you prepared to fill the resulting prescriptions?

Refills alone amount to a tidy sum.

Abbott



**HERE'S AN EASY WAY** for asthmatics to carry NORISODRINE powder and the Aerohalor. Detach Aerohalor mouthpiece, insert *capped* cartridge inside Aerohalor, reattach mouthpiece, put in pocket or purse. This is convenient therapy, ready for use when the need arises.

*Trade Mark for Abbott Sifter Cartridge sold only on prescription.

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# Com-Pen

## PROCAINE PENICILLIN G FOR AQUEOUS INJECTION

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Mixed with Water For Injection, U.S.P., or Isotonic Sodium Chloride Solution, U.S.P., Com-Pen quickly forms a homogeneous suspension. Its particles of procaine penicillin G are uniformly dispersed due to the presence of small amounts of harmless dispersing agents. A minimum of agitation is required prior to aspiration.

*Package Information*

Mixed according to directions, Com-Pen produces a uniform suspension, each cc. containing 300,000 units of crystalline procaine penicillin G. Com-Pen is supplied in: (1) five dose vials containing 1,500,000 units, (2) single dose vials (300,000 units) in individual boxes, and (3) single dose vials in boxes of 50.

### EASILY ASPIRATED

Because of the high degree of subdivision of its procaine penicillin particles, Com-Pen is easily aspirated through a 20-gauge needle prior to injection. Prepared suspensions of Com-Pen may be kept at room temperature for one week, or at refrigerator temperature for three weeks, without significant loss of potency.

### EASILY INJECTED

Com-Pen is easily injected through a 20-gauge needle. Small particle size and a homogeneous suspension make this preparation unusually trouble free. This outstanding feature is especially important in both hospital and office practice. Com-Pen is indicated whenever a repository type of penicillin is called for.

CSC

*C.S.C. Pharmaceuticals* . . . . . A DIVISION OF

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For delayed antiallergic action. Each enteric coated Emplet contains 50 mg. of Benadryl hydrochloride. Supplied in bottles of 100 and 1000 Emplets.

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Each Kapseal contains 50 mg. Benadryl hydrochloride and 10 mg. of ephedrine sulfate. Supplied in bottles of 100 and 1000 Kapseals.

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Just facts about

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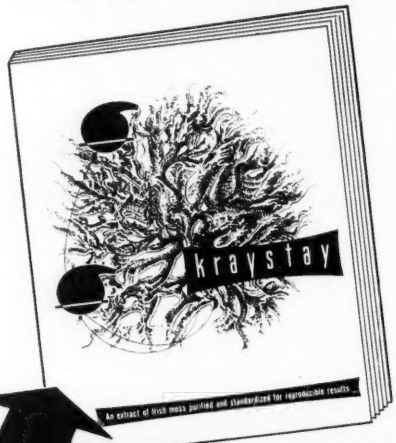


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CALIGESIC® soothes and cools the tenderest skins, promptly relieves sunburn, pruritus, the maddening itch of "poison ivy," or "poison oak," and even diaper rash. Display CALIGESIC with your sunburn remedies, stock it for prescriptions, and in your nursery department—the handy 1½-ounce tube for beach bags and dashboard glove compartments, the economical 4-ounce tube for medicine cabinets. CALIGESIC ointment is greaseless, washes off easily, and contains cool, protective *Calamine*, 8%, analgesic *Benzocaine*, 3%, and antiseptic *Hexylated Metacresol*, 0.05%.
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SHARP & DOHME

for the whole family

*Product descriptions may be clipped and filed on three- by five-inch cards. These are also indexed for quick reference in the "Monthly Drug Index" appearing on the last page of each issue. A product is described in this column for the information of pharmacists who may be asked by physicians to stock the drug, or who may receive professional inquiries about it. A listing does not imply evaluation or recommendation by the Association, nor does omission of any product have significance concerning its merit.*

## ASPIVITE CAPSULES

*Description:* Capsules each containing aspirin 0.3 Gm.; menadione (synthetic vitamin K) 0.35 mg.; and ascorbic acid (vitamin C) 35 mg.

*Form Supplied:* Bottles of 100 and 1000 capsules.

*Action:* Analgesic; vitamins K and C are present to decrease the dangers of hemorrhagic complications and to counteract decrease in the prothrombin content in the blood plasma which may accompany the use of massive doses of salicylates.

*Administration:* Orally, as prescribed by the physician; dosage may vary from one to 30 capsules daily.

*Source:* Sharp & Dohme, Philadelphia 1.

## BACITRACIN OINTMENT AND BACITRACIN OPHTHALMIC OINTMENT

*Description:* Two forms of bacitracin ointment: (1) bacitracin ointment, 500 units per Gm. in 15-Gm. tubes; (2) bacitracin ophthalmic ointment in 4-Gm. tubes.

*Action:* Bacitracin ointment for treatment of pyogenic skin infections; ophthalmic ointment for treatment of external eye infections.

*Administration:* Topically.

*Source:* Abbott Laboratories, N. Chicago, Ill.

## CARMETHOSE-TRASENTINE TABLETS

*Description:* Tablets each containing the antacid demulcent Carmethose (sodium carboxymethylcellulose) 0.225 Gm.; the antispasmodic Trasentine (adiphenine hydrochloride) 25 mg.; and magnesium oxide 75 mg.

*Form Supplied:* Bottles of 100 tablets.

*Action:* Combines antacid demulcent properties of Carmethose and magnesium oxide with antispasmodic properties of Trasentine in treatment of high acidity, hypermotility and spasm in connection with peptic ulcer, gastric neuroses and other forms of gastric dysfunction.

*Administration:* Orally, 2 to 4 tablets four to six times daily.

*Source:* Ciba Pharmaceutical Products, Inc., Summit, N. J.

## CEBETINIC TABLETS

*Description:* Tablets each containing ferrous gluconate 0.3 Gm.; vitamin $B_{12}$ 1 microgram; folic acid 0.67 mg.; thiamine hydrochloride ($B_1$) 2 mg.; riboflavin ($B_2$, G) 2 mg.; pyridoxine hydrochloride 0.5 mg.; nicotinamide 10 mg.; ascorbic acid 25 mg.

*Form Supplied:* Bottles of 60 and 500 tablets.

*Action:* Hematinic in the treatment of iron-deficiency anemias and other anemias that give rise to increased nutritional requirements.

*Administration:* Orally, recommended adult dosage is 3 or more tablets daily.

*Source:* The Upjohn Co., Kalamazoo 99, Mich.

## CEHISTRA TABLETS

*Description:* Effervescent tablets each containing the antihistamine prophenpyridamine maleate 10 mg.; vitamin C 0.1 Gm.; and aspirin 0.32 Gm., in an alkalizing base consisting of sodium bicarbonate (1.82 Gm.) calcium hydroxide and citric acid.

*Form Supplied:* Vials of 10 tablets.

*Action:* Anthistaminic, including treatment of the common cold.

*Administration:* One tablet every three or four hours dissolved in water. Label bears Rx-legend.

*Source:* Organon, Inc., Orange, N. J.

## ESKEL TABLETS (khellin formulation)

*Description:* Tablets each containing a mixture of active principles, chiefly khellin, extracted from the plant *Ammi visnaga*, equivalent to 40 mg. of crystal-

**(*Continued on Page 400*)**

## *a better prognosis for the traumatized or infected eye*

Prompt instillation of SODIUM SULFACETIMIDE SOLUTION 30% following injury to the cornea or conjunctiva is a remarkably certain means of preventing ocular infection. "In 365 eyes in which a foreign body was removed . . . no infection occurred in any case."[1]

When treatment is started early, eye infections such as acute conjunctivitis may be cured within 36 hours.[2] Beneficial results have been obtained in 80 per cent of patients. In corneal ulcer the eye becomes practically normal in three or four days.[3]

# SODIUM SULFACETIMIDE SOLUTION 30%

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In both the treatment and prophylaxis of eye infections, daytime therapy with SODIUM SULFACETIMIDE SOLUTION 30% is best supplemented by using SODIUM SULFACETIMIDE OPHTHALMIC OINTMENT 10%, applied at bedtime to maintain around-the-clock bacteriostasis.

**Dosage:** SODIUM SULFACETIMIDE SOLUTION 30%. One drop instilled in the eye every two to four hours depending on severity of infection or trauma.

**Packaging:** SODIUM SULFACETIMIDE SOLUTION 30% available in 15 cc. eye-dropper bottle. SODIUM SULFACETIMIDE OPHTHALMIC OINTMENT 10% in ⅛ oz. tubes.

**Bibliography:** 1. Mayer, L. L.: Arch. Ophth. *39*:232, 1948. 2. Kuhn, H. S.: Tr. Am. Acad. Ophth. (May-June) 1946, p. 210. 3. Wilkinson, O., in discussion of Mayer, L. L.: Arch. Ophth. *39*:232, 1948.

Schering CORPORATION
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SODIUM SULFACETIMIDE SOLUTION 30%

## NEW PRESCRIPTION PRODUCTS

**Eskel Tablets** • • • • • • • • • *from page 398*

line khellin. [*Note:* Khellin is described in the United States Dispensatory, 24th ed., as a crystallizable principle (a dimethoxy-methyl-furanochromone) probably identical with visammin. Long used in Egypt in the treatment of ureteral spasm and kidney stones, the substance was discovered in 1947 to be an active coronary vasodilator.]

*Form Supplied:* In bottles of 50 tablets.

*Action:* Reported to have vasodilating properties useful in the prophylaxis and treatment of angina pectoris and bronchial asthma.

*Administration:* Orally, as prescribed by the physician. Average dose is 1 tablet three times daily after meals. Relief from anginal pain may be expected in three to seven days. If side reactions (nausea and dizziness) occur, drug should be withdrawn for two or three days.

*Source:* Smith, Kline & French Laboratories, Philadelphia 1.

## FENOXYDYNE COMPOUND TABLETS

*Description:* Tablets each containing the antihistamine Fenoxydyne citrate (chlorothenylpyramine citrate) 25 mg.; acetophenetidin 0.32 Gm.; and caffeine 32 mg.

*Form Supplied:* Bottles of 25, 100, 500 and 1000 tablets.

*Action:* For treatment of the common cold using the combined anthistaminic-analgesic-antipyretic therapy.

*Administration:* Orally, suggested adult dosage is one or 2 tablets every three or four hours for at least forty-eight hours.

*Source:* George A. Breon & Co., Kansas City 10.

## HISTA-CLOPANE PULVULES

*Description:* Pulvules each containing the antihistamine Histadyl (thenylpyramine) 25 mg.; and the vasoconstrictor Clopane (cyclopentamine) hydrochloride 12.5 mg.

*Form Supplied:* Packages of 100, 500 and 5000 pulvules.

*Action:* Indicated in the treatment of the nasal and ocular symptoms of hay fever and vasomotor rhinitis.

*Administration:* Orally, as prescribed by the physician.

*Source:* Eli Lilly and Co., Indianapolis 6.

## KONDRETABS

*Description:* Tablets each containing Irish Moss concentrate 0.25 Gm. (equivalent to 0.625 Gm. of Irish Moss) and methyl cellulose 0.5 Gm.

*Form Supplied:* Bottles of 50 and 100 tablets.

*Action:* Bulk laxative.

*Administration:* One or 2 tablets, three times a day with a full glass of water.

*Source:* E. L. Patch Co., Stoneham, Mass.

## LIPOCAPS

*Description:* Capsules each containing choline bitartrate 0.45 Gm.; *dl*-methionine 0.15 Gm.; and inositol 0.1 Gm.

*Form Supplied:* Bottles of 100 capsules.

*Action:* Lipotropic therapy.

*Administration:* Orally, as prescribed by the physician.

*Source:* Lakeside Laboratories, Inc., Milwaukee 1.

## LITRISON CAPSULES

*Description:* Capsules each containing *dl*-methionine; choline dihydrogen citrate; thiamine hydrochloride; riboflavin; panthenol (a derivative of pantothenic acid); pyridoxine hydrochloride; niacinamide; folic acid; biotin; vitamin $B_{12}$; vitamin A palmitate; and *dl*-alpha-tocopherol acetate.

*Form Supplied:* Bottles of 100 and 500 capsules.

*Action:* Recommended for the prevention and treatment of liver diseases which are responsive to lipotropic factors and fat and water-soluble vitamins.

*Administration:* Orally; a daily dose of 6 capsules is recommended.

*Source:* Hoffmann-La Roche, Inc., Nutley 10, N. J.

## ORADIAL

*Description:* Tablets (2 sizes) containing 0.02 mg. or 0.05 mg. ethinyl estradiol.

*Form Supplied:* Bottles of 30 and 100 tablets.

*Action:* Treatment of estrogen deficiency.

*Administration:* Orally, as prescribed by the physician.

*Source:* Van Pelt & Brown, Inc., Richmond, Va.

## ORESTRALYN

*Description:* Two dosage forms of ethinyl estradiol: (1) tablets 0.02 mg. and 0.05 mg.; (2) elixir containing 0.12 mg. per 30 cc.

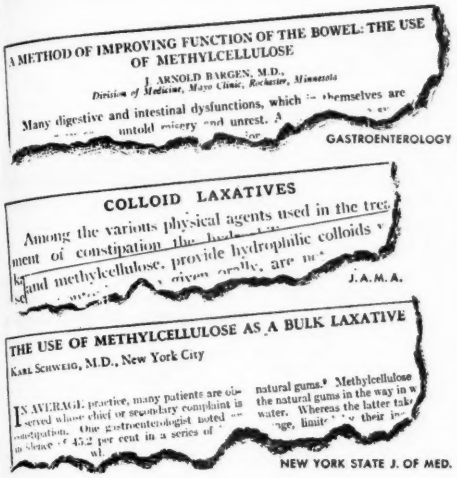
*Form Supplied:* Bottles of 100, 1000 and 5000 tablets; elixir in 4-oz., pint and gallon bottles.

*Action:* Treatment of estrogen deficiency.

*Administration:* Orally, as prescribed by the physician.

*Source:* McNeil Laboratories, Inc., Philadelphia 32.

**(*Continued on Page 402*)**


A METHOD OF IMPROVING FUNCTION OF THE BOWEL: THE USE OF METHYLCELLULOSE
J. ARNOLD BARGEN, M.D.
Division of Medicine, Mayo Clinic, Rochester, Minnesota
GASTROENTEROLOGY
COLLOID LAXATIVES
J.A.M.A.
THE USE OF METHYLCELLULOSE AS A BULK LAXATIVE
KARL SCHWEIG, M.D., New York City
NEW YORK STATE J. OF MED.

# *All in favor of* Cellothyl®

**METHYLCELLULOSE PREPARED BY THE "CHILCOTT PROCESS"**

*to correct constipation*

## WHAT IS CELLOTHYL?

Cellothyl tablets contain *methylcellulose* specially prepared by the Chilcott process for use as a bulk constipation corrective.

It is similar to food cellulose which provides colonic bulk in the normal diet for normal bowel function.

## WHY IS CELLOTHYL RECOMMENDED?

Because Cellothyl tablets can correct years of constipation in days.

*Because* the Mayo Clinic found that even life-long constipation due to bulk deficiency yields to Cellothyl in a week to 10 days.
*Because* Schweig reported "excellent" or "good" results in 92% of cases.
*Because* the J.A.M.A. declared that methylcellulose has "obvious advantages over the natural gums".

## WHERE DOES IT ACT?

Cellothyl corrects constipation at the primary site of constipation—the colon.

Cellothyl passes through the stomach and upper intestines as a liquid. It thickens to a smooth gel in the colon, to provide bulk for a well-formed, easily passed stool. Bloating and distention are avoided.

## WHEN DOES CELLOTHYL ACT?

Time is an important part of Cellothyl therapy.

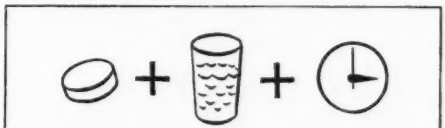
Results can be expected in the time it takes for Cellothyl to pass through the digestive tract to the rectum—usually 16 to 33 hours. In severe cases, a return to normal function may take 7 to 10 days.

## HOW DOES CELLOTHYL PERFORM?

Cellothyl, by its water-retaining properties, converts the dry hard contents of the constipated colon into soft, moist easily passed bulk.

Adequate water must be taken with Cellothyl to facilitate its hydrophilic action. At least a full glass of water must be taken with each dose and fluid intake during the day must be high.

**To correct years of constipation . . . or to prevent chronic constipation from developing:**




Cellothyl is available in tablets in bottles of 50, 100, 500 and 5000.

ACCEPTED COUNCIL ON PHARMACY AND CHEMISTRY AMERICAN MEDICAL ASSOCIATION

CHILCOTT Laboratories DIVISION OF The Maltine Company

®REG. U. S. PAT. OFF. MORRIS PLAINS, NEW JERSEY

## NEW PRESCRIPTION PRODUCTS

• • • • • • • • • • • • • • • • • • • • *from page 400*

### RETICULEX PULVULES

*Description:* Pulvules each containing liver-stomach concentrate 0.4 Gm.; ferrous sulfate, anhydrous 0.2 Gm.; ascorbic acid 50 mg.; folic acid 0.33 mg.; and vitamin $B_{12}$ 10 micrograms.

*Form Supplied:* Bottles of 100, 500 and 5000 pulvules.

*Action:* Indicated in the treatment of many forms of commonly encountered anemia.

*Administration:* Orally; suggested average dose is 2 pulvules three times daily.

*Source:* Eli Lilly and Co., Indianapolis, 6.

### SUGRACILLIN GRANULES

*Description:* Flavored granules of buffered crystalline penicillin G potassium, packaged in 60-cc. bottle.

*Form Supplied:* 60-cc. size bottle contains 1,200,000 units penicillin. Can be stored at room temperature before dissolving.

*Action:* Oral penicillin therapy.

*Administration:* Contents of bottle are dissolved in enough water to make 60 cc. of solution (100,000 units per teaspoonful). Initial dose is usually 500,000 units followed by 100,000 units every three hours.

*Source:* The Upjohn Co., Kalamazoo 99, Mich.

### TESTRONATE

*Description:* An aqueous suspension of pure crystalline testosterone containing 25 mg. per cc.

*Form Supplied:* 10-cc. rubber capped vials.

*Action:* Indicated in male hormone therapy.

*Administration:* Recommended dosage for beginning treatment is 25 mg. three times weekly.

*Source:* Smith-Dorsey Co., Lincoln, Nebr.

### THROMBODENT DENTAL CONES

*Description:* Dental cones each containing 1 unit of human thrombin (sufficient to clot 1 cc. of normal blood in less than one minute), combined with 1 mg. of tyrothricin.

*Form Supplied:* Bottles of 12 and 50.

*Action:* Aids in clot formation by maintaining thrombin at the bleeding point following tooth extraction.

*Administration:* Topically, as administered by the dentist.

*Source:* Sharp & Dohme, Inc., Philadelphia 1.

### VERILOID

*Description:* 1-mg. tablets containing the hypotensive ester alkaloids of *Veratrum viride* obtained by extraction.

*Form Supplied:* Bottles of 100 and 200 tablets.

*Action:* Vasodilator.

*Administration:* Orally, as prescribed by the physician.

*Source:* Riker Laboratories, Inc., Rexall Drug Co., Los Angeles.

### VISTORA TABLETS

*Description:* Effervescent tablets each containing aspirin 0.32 Gm.; vitamin C 0.1 Gm.; sodium bicarbonate 1.82 Gm.; calcium hydroxide; and citric acid.

*Form Supplied:* Vials of 10 tablets.

*Action:* Analgesic and alkalizing.

*Administration:* Orally, dissolved in water. Average dose is 1 or 2 tablets three or four times a day.

*Source:* Organon, Inc., Orange, N. J.

## *Other New Products*

**(Chemicals, clinical trial drugs, diagnostic aids and equipment)**

### Bumintest

A reagent tablet containing sulfosalicylic acid for use by the physician as a test for albuminuria. Available in bottles of 32, 100 and 500. *Manufactured by:* Ames Co., Inc., Elkhart, Ind.

### Cortone (cortisone)

Cortone (trade name for cortisone) will be available early in July to hospitals having certain minimum facilities, including hospitals registered by the American Medical Association. The drug is to be used, during the initial period of treatment, only in patients hospitalized in these institutions. This stipulation is considered essential for the present by the Food and Drug Administration for safe use of the product. Available to qualified hospitals in packages of 3 vials, each vial containing 0.3 Gm. of Cortone. *Manufactured by:* Merck & Co., Rahway, N. J.

### Dibenamine

Dibenamine hydrochloride, a sympatholytic and adrenolytic agent, is now undergoing research at Smith, Kline and French Laboratories, Philadelphia 1. The product was formerly manufactured by Givaudan-Delawanna, Inc., Delawanna, N. J.

### Terramycin

Terramycin is now available in vials of three capsule sizes: twenty-five 50-mg. capsules; twenty-five 100-mg. capsules; and sixteen 0.25-Gm. capsules. *Manufactured by:* Chas. Pfizer & Co., Inc., Brooklyn, N. Y.

# SUMMER WEATHER

BRINGS
INCREASED SALES
OF

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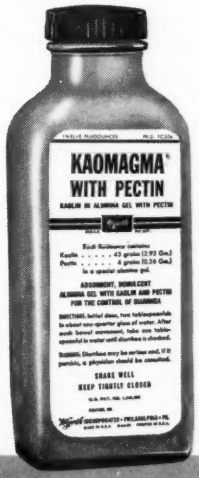


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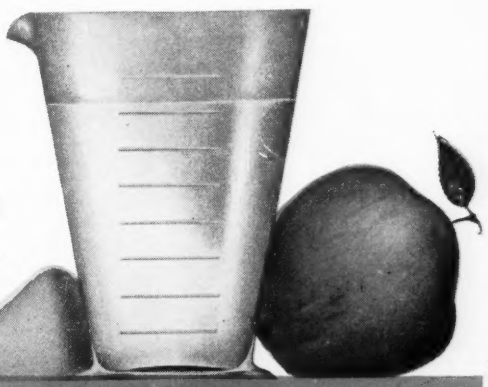

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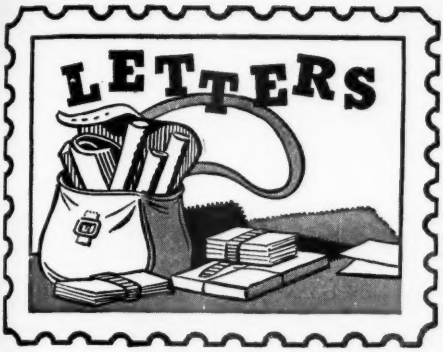


### More Education in Pharmacy?

*On behalf of a past president of the A. Ph. A., a member has submitted a letter written in 1837 that is as expressive in today's concern over the 4-5-6 year curriculum question as it was advanced for its own day.*
—THE EDITOR

To the Editor:

When some of us . . . were engaged in founding the [Philadelphia] College of Pharmacy we were told by many who refused to join us, that we were raising up a set of young men to take the business out of our hands. I told them that I did not fear the result; that we *would* educate a race of young men better instructed than ourselves, and that if we should be forced by their competition to reform our own shops and to review our old studies, both we and the community would be the gainers. I am sure that I was right in my opinion, and that a confidence in sound first principles did not on this occasion lead into any error.

*American Journal of Pharmacy*,
9-97(1837.)

DANIEL B. SMITH
First President of
the A. PH. A.

### Mission to Japan——Follow-through

Sirs:

On Sept. 23, last year, the delegation's report [Mission of the AMERICAN PHARMACEUTECAL ASSOCIATION] was delivered to us from Brigadier General Crawford F. Sams, of the Public Health and Welfare Office, GHQ, SCAP. Today we are able to proceed into the field of our new objectives with a more firm step.

At present I am the head of the pharmacy department of a national hospital in a little town of northern Japan. Of course, my pharmacist office has pharmacy room, laboratories, and pharmaceutical rooms, and these are improving day by day. I am trying my best to bring forth the best results.

Recently, the Welfare Ministry held a lecture meeting regarding the administration of hospitals, and at present the procedures published in "Hospital Organization and Management" by Malcolm T. MacEachern are being transacted in our hospitals. But there was no special reference for the management of pharmacist office, therefore we are now undergoing many hardships, and are solving our problems through our own experiences.

Medical literature from America is not easy to obtain these days and our town being located in such remote region, we must face many difficulties in order to obtain them. This is our present circumstance. Therefore, I wish to make a request for some recent references concerning various prescriptions of hospital use, prescriptions for hospital registration (appointment), and materials for pharmacy.

I believe that, in the future, there will be other problems and matters in which I may again beg for your favor. I will appreciate very much your kind advice, information, and assistance.

Mura Matsu National Hospital ROKURO HARA
Muramatsu-Machi
Nakakanbaragun Nigotaken, Japan

*Note: Information about the Division of Hospital Pharmacy of the A. Ph. A., copies of the Bulletin of the American Society of Hospital Pharmacists, and reprints of articles pertaining to hospital pharmacy have been sent to Mr. Hara.*—THE EDITOR

### Atlantic City to Puerto Rico

Sirs:

On May 15 Dr. C. O. Lee reported on the A. PH. A. Convention before the Puerto Rico Branch of the ASSOCIATION. It was interesting indeed.

We hope Dr. Leo B. Lathroun of Maryland will be here to conduct our next conference which will be our branch contribution to the convention of the "Colegio de Farmaceuticos de Puerto Rico." The topic will be "Who are the pharmacists of the Americas?"

At that time, too, we expect to have a report from our Dr. Torres Diaz who represented us at the Atlantic City Convention.

Santurce, Puerto Rico ADOLFO F. LEGRAND

### Information, Please, and Thank You!

Sirs:

Within the last year we have written you on numerous occasions for information on various pharmaceutical problems. Each time you have given us a prompt answer.

Recently we inquired about an ointment of nitroglycerin and you relayed this information to us by wire. We appreciate very much this service and enclose a contribution to cover the cost of the wire and ask that the balance be placed in the fund sustaining the Information Service Department of the JOURNAL. We are aware that the amount is small but we hope that it will convey to you our appreciation for the service you have given.

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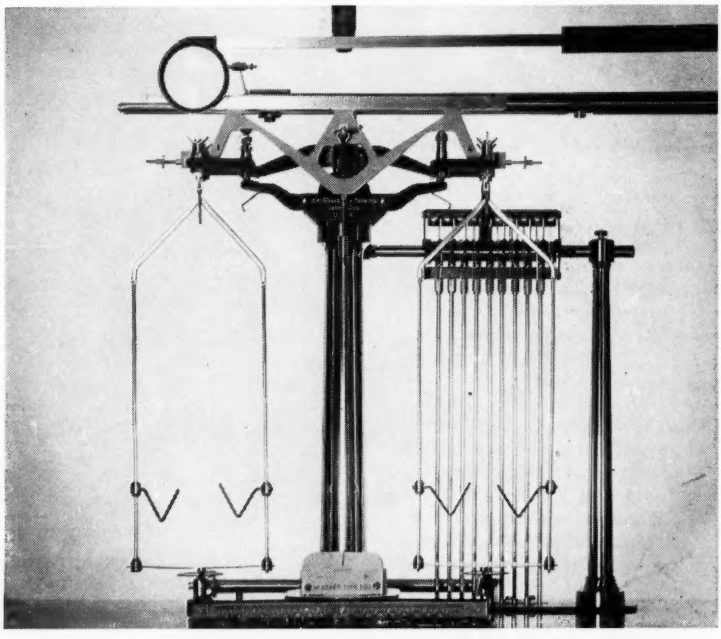

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Journal of the

# AMERICAN PHARMACEUTICAL ASSOCIATION

VOL. XI. NO. 7.
NSECUTIVE NO. 13

Practical Pharmacy Edition

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THE COVER

N. F. IX, official November 1, 1950, is ready now for distribution. The A. PH. A.'s first edition *National Formulary of Unofficial Preparations* was published in 1888. See Page 420 for story of the ninth edition.

## JULY, 1950

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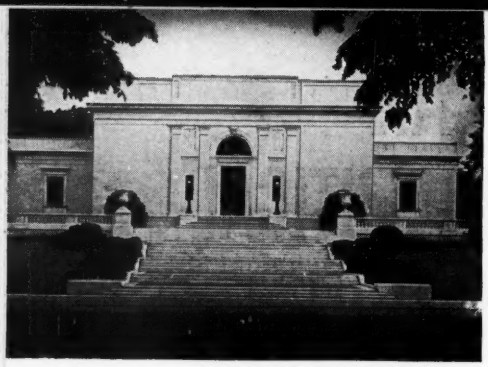


# STRAIGHT FROM HEADQUARTERS

By *ROBERT P. FISCHELIS*, Secretary
AMERICAN PHARMACEUTICAL ASSOCIATION

## The New National Formulary

Elsewhere in this issue of THE JOURNAL, Dr. Justin L. Powers, chairman of the Committee on National Formulary, writes interestingly about the new National Formulary IX.

To those who have little time to give thought to the production of books of standards like the U. S. P. and N. F., their appearance at regular intervals is not apt to cause any excitement. But to those who must review each of the monographs with meticulous care to make sure that the standards for the drugs described are stated with accuracy and represent methods of determining identity, purity, and strength which will stand up under critical conditions, the completion of such a book marks the end of a task well performed. It also marks the beginning of another revision.

Continuous revision of these standards is required because of the rapid progress that is being made in the sciences which contribute to medicine and pharmacy. The AMERICAN PHARMACEUTICAL ASSOCIATION points with pride to the fact that since 1888 it has produced this important book of standards for drugs and that since 1906 this volume has been one of the official standards for drugs under Federal and State Food, Drug, and Cosmetic Acts. Much of the service of the ASSOCIATION rendered at its headquarters building by its laboratory and its editorial staff goes into the development of improved drug standards. To all who have contributed to the development of the National Formulary, to the Committee of Revision of the National Formulary and its sub-committees and especially to its chairman, the ASSOCIATION extends congratulations and thanks. The National Formulary IX becomes official November 1, 1950. An order form will be found on Page 452.

## Hospital Pharmacy Progress

THE enthusiasm with which hospital pharmacists go about their work these days is an indication of the progress that is being made in this specialty. Not only are hospital pharmacists enthusiastic about their work because of the greater opportunity that is being developed for them to practice their profession but also because they instinctively feel that more and more there is recognition of their importance to the welfare of patients and to the success of the hospital with which they are associated.

The AMERICAN PHARMACEUTICAL ASSOCIATION takes considerable pride in what has been accomplished in the past five years for hospital pharmacy. Hospital pharmacists in turn can take pride in what they have accomplished toward the advancement of the profession in which they are such an important factor.

No other specialty within the framework of American pharmacy has had such a rapid growth and no group of pharmacists has accepted any better the challenge of the changing order in providing improved medical care for more people.

It is important that colleges of pharmacy recognize the rapid strides which are being made in hospital pharmacy and provide the necessary educational opportunities for basic training leading to careers in hospital pharmacy. It is likewise important for

hospitals to provide adequate facilities for the development of a pharmaceutical service that will take full advantage of the training and abilities of hospital pharmacists to supply a high quality of service to both staff and patients.

It is interesting to observe that, while hospital pharmacy is an old and long-established specialty within the field of pharmacy, the present leadership is in the hands of comparatively young members of the profession whose training has been received in the era of synthetic medicinals and antibiotics. There is nothing static about this group. They are thinking and planning in terms of making hospital pharmacy ever more useful to hospital administration, to physicians, and to patients. In doing so, they are inevitably making it more satisfying and remunerative to themselves.

More than 150 of the best hospital pharmacists in the country took part in the Sixth Institute on Hospital Pharmacy offered jointly by the American Hospital Association, AMERICAN PHARMACEUTICAL ASSOCIATION and American Society of Hospital Pharmacists at Ann Arbor, Michigan, in June.

More than fifty attended the second of such institutes sponsored by the Catholic Hospital Association in cooperation with AMERICAN PHARMACEUTICAL ASSOCIATION and American Society of Hospital Pharmacists at Milwaukee last month.

The eagerness of hospital pharmacists to keep abreast of developments in all phases of medical, pharmaceutical, public health, and hospital practice shows up to best advantage at these institutes. They are addressed by outstanding specialists in hospital administration, medicine, pharmacy, and related activities. The members of the institute take part in the lively discussions, which follow the presentation of the many and varied subjects. They go back to their respective institutions at the end of a week of study, discussion, and recreation, refreshed in mind and spirit because of their pleasant contacts with men and women who are daily confronted with the same problems that confront them. They have also had opportunity to explore minds applied intensively to the solution of special problems.

They are inspired to give more and better service to the sick, and they have provided some of that same inspiration to others.

To anyone who has never attended such an institute, a word picture of its activities and effects is totally inadequate. Here we experience and become a part of pharmacy in its noblest conception. It is this type of "post-graduate" and refresher education which the pharmaceutical survey had in mind when recommending continuation study for practicing pharmacists.

## A Loss to American Pharmacy

The death of Dr. William F. Snow, one of the founders and for many years the director of the American Social Hygiene Association, reported on another page of this issue of THE JOURNAL, is a distinct loss to American pharmacy as it is a great loss to American medicine in its contacts with the public on the social hygiene front.

Dr. Snow, who started his career as a teacher at Stanford University, spent most of his professional life in dealing with problems of public health. For the greater part of World War I he was on General Pershing's staff, assigned to dealing with the venereal disease problem in the expeditionary forces and in World War II he contributed much as a consultant to the military forces. Between the wars and throughout his entire professional career, Dr. Snow stimulated groups of citizens who fought the evils of prostitution and worked for a better understanding of the problems of sex and family life.

He was among the first to recognize the importance of pharmacists in dealing with the venereal disease problem and he was enthusiastic about the cooperation of the AMERICAN PHARMACEUTICAL ASSOCIATION and the Social Hygiene Association in working out programs utilizing the retail pharmacy as a source of information leading to proper treatment for those who apply to pharmacists for aid in the prevention and cure of venereal disease.

His great contributions to the field in which he spent so many productive years have been recognized nationally and internationally. We desire to pay tribute to his untiring zeal for the development of better health and his continuous effort toward conquering the venereal disease evil.

The AMERICAN PHARMACEUTICAL ASSOCIATION joins the American Social Hygiene Association in mourning the loss of one who was ever willing to sacrifice his own comfort and convenience for the welfare of his fellow men.

# The present status and probable future developments of CORTISONE ACTH and related compounds

by Norman H. Topping, M.D.

Assistant Surgeon General, Public Health Service, Federal Security Agency; Associate Director, National Institutes of Health

I DEEPLY appreciate this opportunity to address the members of the AMERICAN PHARMACEUTICAL ASSOCIATION at its Mid-Century Convention.

As your Secretary, Dr. Robert P. Fischelis, has pointed out, "Of all the professions in the health field, pharmacists are the ones who contact people most extensively when they are in good health as well as when they are sick..... American pharmacists make five billion or more contacts each year with the people of the United States—a logical reason why the corner pharmacy can serve a useful purpose as a health education center"(1).

In serving the people of the United States, pharmacists undoubtedly have had to answer countless questions on the efficiency and toxicity of the sulfonamides and antibiotics; on the status of penicillin, streptomycin, aureomycin, and many others of the remarkable list of chemotherapeutic agents developed in recent years.

Today, the victims of a dozen ailments—from arthritis to rheumatic fever—eagerly await news concerning the latest "wonder drugs"—cortisone and ACTH. They write thousands of tragic letters to the government, they ask their doctors, and I am sure they have asked their pharmacists uncounted times for the facts about these new medicines.

And what can we, in all frankness, tell them? What is the current status of cortisone and ACTH? When will an adequate and less expensive supply of these new drugs be generally available? What are the good and bad results of treatment?

Hundreds of scientists have sought answers to these questions in scores of studies (2, 3) over the past year or so. A great deal more investigation will be required before the role of the adrenal gland in health and disease is thoroughly understood.

Many of us who have closely followed de-

Presented at the Second General Session, AMERICAN PHARMACEUTICAL ASSOCIATION, 1950 meeting, Atlantic City.

velopments in the laboratory and clinical trials will be inclined to agree with the recently expressed views of the Council on Pharmacy and Chemistry of the American Medical Association. The Council believes that in the present state of our knowledge it would be extremely undesirable to encourage the widespread use of these potent preparations in the routine practice of medicine, and that it is perhaps fortunate that neither drug is now available in unlimited quantities (4).

But regardless of whether cortisone and ACTH prove effective in the clinical treatment of disease, they have provided us with important tools to carry on basic medical research in a score of diseases. Even the first preliminary reports have given us new clues. Other studies are helping us learn more about the nature, cause, prevention and cure of mankind's most baffling diseases—some of which have defied science for centuries. Because of their importance in fundamental research, cortisone and ACTH rank among the greatest advances in the history of medicine.

### Early Investigations

Now just what is cortisone—and ACTH? How did these great discoveries come about? How did the investigations of a few scientists like Dr. Philip Hench and Dr. Edward C. Kendall revolutionize our concept of broad areas of disease—and perhaps prepare the way for a new era in medicine?

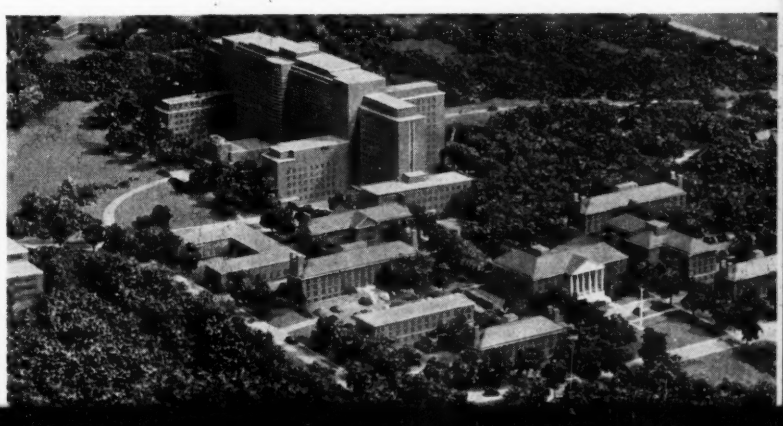
A chemical and physiological investigation of the adrenal cortex begun some twenty years ago in the laboratory of the Mayo Foundation resulted in discovery of a group of new compounds. They were designated A, B, C, D, E and F (5). Compound E was first isolated by O. Wintersteiner and others. It was discovered alone or concurrently by Reichstein in Switzerland.

The chemical structure of these compounds was established, and four of them—A, B, E and F—were found to have physiological activity when tested with laboratory animals. The results of physiological investigation were interesting, but the supply of the compounds was so limited it was not possible to extend their use to human beings. Out of these studies came desoxycorticosterone acetate, useful and practical in the treatment of Addison's disease.

During these same years, similar chemical investigations were being made by Pfiffner and Wintersteiner, in this country, and Reichstein and his associates in Switzerland, but there was no great interest in the commercial production of these compounds for clinical use until the last war. Then it was rumored that through the administration of adrenal gland extracts the pilots of the German air force were enabled to fly and fight efficiently at altitudes of forty thousand feet (6).

Stirred into action, the National Research Council called a conference in Washington to explore the possibilities for manufacture of these compounds in greater quantity. The work of scores of scientists was coordinated and pooled. In 1944 a practical method to make Compound A was devised. Among members of this team were scientists at Merck and Company. In 1946 trials on animals were extended and it was found to be of value in protecting them against poisons and cold. Although these studies confirmed earlier findings, Kendall states that when Compound A was given to a patient whose adrenal gland had been destroyed by disease, it was found to be valueless.

Compound E, later named cortisone by Kendall, was available in sufficient amounts for limited clinical use in the summer of 1948. It was tried on a patient whose adrenal glands had been destroyed by disease and was found to be highly active. By one



*Architect's model of the National Institutes of Health, Bethesda, Md., showing the Clinical Center, now under construction. The Center is to be completed approximately July, 1952.*

of those quirks of chance, with which advances in medical research are sometimes bound up, another Mayo scientist, Dr. P. S. Hench, for twenty-five years had been looking for a drug which would help his arthritis patients. Having observed that patients with rheumatoid arthritis who became jaundiced or pregnant were relieved of their pain, due to a change in steroid metabolism, he decided to try Compound E on several patients with rheumatoid arthritis (7).

The spectacular results with 16 patients suffering from rheumatoid arthritis were announced publicly in the spring of 1949.

Essentially similar clinical results accompanied by various biochemical effects were obtained from the administration of ACTH (pituitary adrenocorticotrophic hormone) to 2 patients at the same time (8).

The authors of the report suggested also that these adrenal and pituitary hormones might be useful against other rheumatic diseases and against certain nonrheumatic conditions. Subsequent work has proved the validity of their suggestion.

Since 1946 the Armour Laboratories has made available its preparation of ACTH to researchers to ascertain the properties of this hormone in the human being. Dr. George W. Thorn and his colleagues were among the first to study ACTH clinically. Shortly thereafter Fuller Albright and his colleagues carried out similar studies.

### Biochemistry

Before describing later events let me review very briefly the chemical and biological facts of cortisone and ACTH.

Cortisone is a complex steroid produced in minute quantities by the adrenal glands of both man and animals. It is one of at least 28 steroids that have been isolated in crystalline form from the adrenal cortex. Cortisone can be synthesized from another complex compound—desoxycholic acid—which is found in the bile of animals.

ACTH, adrenocorticotrophic hormone, is a complex protein produced in the anterior pituitary. Unlike cortisone, ACTH cannot as yet be synthesized but is extracted for medical purposes from the pituitary glands of animals.

ACTH is now under investigation in about 100 clinics where a great many different diseases are being studied. First reports from these studies have indicated encouraging results in some cases.

Let me point out that these are suggestive findings only. Much study will be required before we can appraise the results and obtain definite conclusions.

There are preliminary indications that ACTH may terminate an episode of rheumatic fever and, with suitable continuation therapy in conjunction with antibacterial agents, stop further progress of the disease. But we should not be too optimistic about these first reports.

ACTH has also been reported to bring under control lupus erythematosus (a serious metabolic disease), and congenital hypoglycemia (low blood sugar) in some cases.

It is reported that some common skin diseases, including psoriasis, have been cleared up by ACTH within several days.

Several reports have suggested that ACTH has been of some value in the control of asthma, hay fever and other allergic ills.

Once again, I emphasize these are only preliminary findings and require more research.

ACTH also is described as being able to counteract sensitivity to penicillin (a sensitivity which may limit the use of this important drug in sensitive persons).

At least one investigator has reported that ACTH might help modify the course of disease in two kidney complaints—nephritis and nephrosis.

When used on certain types of mental illness, ACTH produces measurable changes in the brain wave patterns.

A few reports have stated that some patients suffering from leukemia and cancer of the lymph glands showed dramatic and progressive improvement after administration of cortisone and ACTH. These are temporary effects. However, the cancers were not refractory to a second course of therapy, which is unusual in cancer therapy.

It should be emphasized again that these reports are only preliminary. In most cases they involve only a small number of cases, observed over a short period of time. Much additional research remains to be done before there will be a scientific basis for belief that cortisone and ACTH are effective treatment for many of the above-mentioned diseases. On the basis of present reports, cortisone and ACTH definitely cannot be regarded as a cure for cancer.

Most reports suggest that in chronic diseases, as in the case of insulin, treatment by cortisone and ACTH must be continued or the patient will relapse.

### Toxicity Studies

Chronic toxicity studies on these two compounds are still far from complete, but they indicate that regular administration at present dosage schedules of either preparation over a long period often cannot be tolerated.

Another hazard in the prolonged use of cortisone and ACTH is the accompanying disturbance of the pituitary-adrenal system.

ACTH stimulates the adrenal and appears to have a depressant effect on carbohydrate metabolism. Although studies are inconclusive, there is some evidence that continued use of ACTH might lead to diabetes of a high insulin-resistant type. Hypertension has also been noted in individuals treated with ACTH.

Many patients using cortisone and ACTH in high dosage or over a long period of time develop some of the symptoms of Cushing's disease. They may develop acne, growth of hair, rounded facial contours, and some indication of sex and personality changes. The early feeling of well-being noted by some patients may later give way to depression (9). When the administration of these drugs is discontinued there may be a rebound effect, the initial symptoms of the disease recurring with even greater severity than before (10).

It is reasonable to believe that some of these complications can be prevented. Others, such as development of some of the signs of Cushing's syndrome, may prove to be less serious than they are thought to be at present. But the fact that these complications have been encountered necessitates considerable caution in accepting ACTH and cortisone into general therapeutic usage at this time (11).

Much of the current research in our medical schools, hospitals and research centers is devoted to finding ways of avoiding or minimizing these side effects (12, 13). But let me emphasize the rapidly changing nature of the cortisone problem. What may be significant today may be completely outmoded tomorrow. We are constantly obtaining new reports from investigators. Only the other day, Dr. Chester S. Keefer of the Evans Memorial Hospital, Boston, Chairman of the Committee on the Investigation of Cortisone of the National Academy of Sciences, reported that in 100 patients who received doses of 100 to 200 mg. daily for seventy days, the side effects were minimal and always reversible (14). It is evident that more study will be needed before we can fit together all these varied pieces in the cortisone-ACTH puzzle.

### Availability

Cortisone and ACTH now are available only in hospitals and clinics where completely controlled, metabolic studies of the patient can be made. The drugs should be used only after the patient understands fully the dangers involved (15).

At present the large-scale production of cortisone and ACTH for clinical use is the most urgent aspect of the problem. However, enough is now being produced to carry on research. The only company which is producing cortisone on an important scale—Merck and Company—may be able to supply by the end of 1950, at most, enough to care for a fraction of the estimated 7 million persons (16) who suffer the types of arthritis and rheumatism which appear to benefit from cortisone.

A committee of the National Academy of Sciences, acting for Merck and Company, orginally distributed cortisone to qualified investigators without charge (17). Since January 1, 1950, the company has taken over the distribution and sale of cortisone. Armour Laboratories has been allocating its small supply of ACTH to qualified institutions and individuals, and now Wilson and Company are distributing their product in a similar manner.

In a joint meeting with the Surgeon General on February 18, the five National Advisory Councils—which regularly advise the Public Health Service on the problems of general medical research—praised the private manufacturers who have spent millions of dollars to develop these drugs, and who up until recently have made them available to scientists without cost. The financial burden on these private concerns has become so great that they are now compelled to charge the cost of production.

I am sure all of us deeply appreciate the humanitarian efforts of these manufacturers in making the compounds available to qualified research workers.

In the opinion of the National Advisory Councils, the most important single medical problem facing the country today is how to insure that the drugs will continue to be available to research workers. If this is not done, the full benefit to humanity of one of the greatest developments in medical history will be delayed for several years.

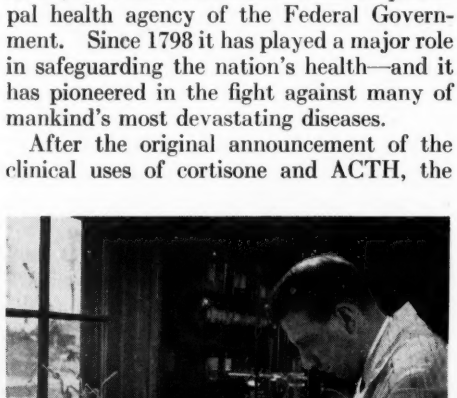
The Councils therefore urged that research be expanded by hospitals, medical schools, universities and by both public and private research laboratories. However, the group emphasized that this expanded research in hormonal compounds should be "additive." In other words, that it should not be at the expense of other important types of medical research in such fields as cancer, heart disease, infantile paralysis, and so on.

In order that research involving ACTH, cortisone and related compounds may proceed with maximum speed and effectiveness, the Councils felt that a program to correlate the numerous projects of governmental and private institutions was needed (18).

### Role of U. S. Public Health Service

Now where does the U. S. Public Health Service come into the picture? As you know, the Public Health Service is the principal health agency of the Federal Government. Since 1798 it has played a major role in safeguarding the nation's health—and it has pioneered in the fight against many of mankind's most devastating diseases.

After the original announcement of the clinical uses of cortisone and ACTH, the Public Health Service consulted with scientists prominent in this field; with other Federal agencies, particularly the U. S. Department of Agriculture; and with pharmaceutical manufacturers concerning possible means of increasing the supply of these drugs.



*Fractionation of final products from Strophanthus as performed at the Experimental Biology and Medicine Institute of the National Institutes of Health.*

Since animal source of the starter material for cortisone is obviously expensive, the search naturally has turned to plants as a basic source of supply. Several domestic and foreign plants are being investigated. For example, the strophanthus plant contains steroid compounds which may lend to less complicated processing. It is estimated that a ton of strophanthus seed is equivalent to 12,500 animals in cortisone production.

However, the strophanthus plant is not native to the United States and requires five years to come to seed. An expedition sent jointly by the Public Health Service and the Department of Agriculture has secured strophanthus material from Africa.

At the National Institutes of Health in Bethesda, Maryland, the Public Health Service is undertaking the synthesis of cortisone from these strophanthus seeds, and from leaves of digitalis lanata and other types of plant species.

Other researchers have found some 200 species of plants from which sterol-yielding sapogenins can be obtained, one or more of which, it is hoped, may provide an easily available source of cortisone. These include the common agaves, yuccas, and dioscorea or Mexican yams. These are hardy plants which grow luxuriantly.

Synthetic substances, structurally similar to cortisone, are being investigated in a number of laboratories and clinics.

While the nation's laboratories and medical schools are working to find easier ways to produce cortisone and ACTH in quantity, they are at the same time at work on related compounds of simpler chemical structure which give early indications of being effective in treatment.

Investigators are now carrying on research on a number of compounds which, it is hoped, may eventually supplant cortisone and ACTH. These include (1) acetoxypregnenolone; (2) pregnenolone; (3) desoxycorticosterone acetate; (4) testosterone, and several others.

On April 1, a new and more powerful form of the hormone ACTH, developed by Ast-

wood at the Ziskind research laboratories of the New England Medical Center in Boston, was reported to be 30 times as potent as the "Armour Standard." Dr. Samuel Proger, Chief of Staff of the Center, said it had been prepared in limited quantities, that it produced no ill effects and was therapeutically effective (19, 20).

Investigators have broken up the complicated ACTH molecule into a number of small polypeptides, and tests have shown that these peptides still retained the power of the whole molecule in giving relief from the ravages of the disease (21). Since peptides have a much smaller molecule than the ACTH protein, the findings open up the possibility of synthesizing substances with ACTH-like activity.

A report was presented at a symposium on the adrenal gland cortex at the annual meeting in December, 1949, of the American Association for the Advancement of Science by Dr. Laurence W. Kinsell, and his associates, Dr. Sheldon Margen, Dr. George Michaels and Dr. Choh Hao Li, of the University of California.

Incidentally, the basic chemical work of Kinsell and his associates at the University of California, and the work of Astwood in Boston were—and still are—supported by grants from the National Institutes of Health.

Investigators at the Worcester Foundation for Experimental Biology are seeking ways to retain viability of adrenal glands by perfused techniques in glass vessels and obtain their secretions. These researchers have demonstrated that when desoxycorticosterone is supplied in the circulating fluid, the gland produces Kendall's Compound F (22).

I might add that the work carried on at Worcester also is supported by a grant from National Institutes of Health.

Scientists at the National Institutes of Health have also pioneered in the development of new tissue culture techniques which hold promise of opening up unexplored fields of research. They have succeeded in developing actively growing cultures of cells derived from the pituitary glands of rats. About 130 glands have been successfully grown outside the body—some for as long as ten weeks, and there is every indication that they can be maintained for a much longer period. These gland tissues are actively producing hormones, as demonstrated by actual bioassay on experimental animals. Among those are substantial yields of sex-stimulating hormones and ACTH.

*Purified aglycone (steroid nucleus) from Strophanthus*

Work on this project has been going on for over a year, but it is still definitely in the experimental stage. The fluids on the growing tissues are being replaced three times a week and the drained-off fluid has been found to contain appreciable quantities of various pituitary hormones. Progress to date encourages further effort toward the development of newer techniques which may lead to the mass production of these medicinally important substances by means of tissue culture.

### New Era in Medicine

It is evident that the clinical use of ACTH and cortisone has opened up a new era in medicine. Only a few weeks ago investigators found that the administration of ACTH may help determine whether a patient will be a good surgical risk.

Dr. M. Roche and G. W. Thorn of Peter Bent Brigham Hospital and Harvard Medical School in Boston, and Dr. A. G. Hills of the University of Pennsylvania Hospital and Medical School, Philadelphia, reported that if there is a marked fall in number of eosinophils four hours after administration of ACTH, the patient probably will come through the operation satisfactorily (23). However, if there is no drop in eosinophil blood cells, the risk of operation is great because the patient probably does not have the necessary reserve power in his adrenal glands.

The Public Health Service, through the

National Institutes of Health grants program, is actively interested in increasing the supply of cortisone and ACTH and of our knowledge of their effects and mode of action.

During the past few months, for example, the National Institutes of Health awarded 102 financial grants—totaling $901,445—to universities, medical schools and other non-Federal institutions to carry on intensive research in these new drugs.

### Research Projects

Let me indicate just a few of the projects which Public Health Service grants are aiding in the nation's research centers:

In addition to furthur research on the effect of cortisone and ACTH on rheumatoid arthritis and related conditions, N. I. H.-aided investigators are studying the effect of these drugs on allergic hypersensitivity, chronic sinusitis, the cause of diabetes, renal function, cirrhosis, and hypertensive vascular disease. Other investigators are studying the effect of these drugs on circulation, acute rheumatic fever, fat metabolism and nutrition.

The pathogenesis and treatment of gout, psychosomatic reactions of stress as a function of age, and the detection of patients with potential diabetes mellitus are some of the other important investigations now in progress with the support of P. H. S. grants.

Another project will study the use of cortisone in treating tuberculosis. The effectiveness of cortisone in treating eye disease is also under investigation.

Other Public Health Service supported research includes studies of steroid hormones in chronic liver disease; the relation of pituitary and steroid hormones to normal and abnormal growth; the relation of amino acid metabolism to rheumatoid arthritis, and the role of the adrenal cortex in rheumatic fever. Cortisone and ACTH are also being utilized in studies of cancer and other degenerative diseases.

In addition to awarding research grants to non-Federal institutions, the Public Health Service has assigned many of its best scientists to carry on investigations in these fields in the laboratories of the National Institutes of Health. These projects, of course, vary widely. They include basic investigations on the physiological effects of the steroids. Here, again, much more research will be required before we have definite results.

The infectious agents which we hope to study in the months ahead include a variety of viruses and rickettsia, the brucella, various streptococci, and the acid-fast bacilli, as well as such animal parasites as the *schistosomes*, the *trypanosomes*, the *amoeba*, and the *leishmania*. Host animals under study in the laboratories range from invertebrates such as snails, triatoma and most quitoes to the common laboratory animals such as mice, guinea pigs and monkeys.

In addition, the National Institutes of Health are studying the effect of aging on the adrenal response to ACTH and the effect of cortisone on spontaneous and transplanted leukemia, lymphomas and tumors in mice.

We are planning to carry on experiments with steroid hormones in pregnant rats and hope these hormones may induce an eclampsia-like condition. It is thought by some that the cortex of the adrenal plays a role in this condition. We hope that these experiments may give us valuable clues to the pathogenesis and treatment of eclampsia.

It will be some time before we can report our findings.

Of course, our work with the hormones represents only a portion of the research we are now carrying on at the National Institutes of Health.

### Activities of the National Institutes of Health

Since its establishment in 1887, the principal research arm of the Public Health Service has advanced knowledge in nearly all fields of medical science. N. I. H. laboratories and field stations today are among the finest and largest in the world; these facilities will be greatly expanded when our 14-story, $40,000,000 Clinical Center, now under construction in Bethesda, is opened in July, 1952.

Major emphasis will be placed on the investigation and treatment of cancer, heart disease and mental disease—now the greatest causes of illness, disability and death in our population. Plans for the new 500-bed Clinical Center incorporate hospital facilities of the most modern design and laboratories with a wide range of flexibility for study in the biological and physical sciences.

Integration of fundamental and clinical

research will afford many opportunities to advance methods of diagnosis and treatment and to study the cause and possible prevention of many degenerative diseases. Patients from all parts of the country will be referred for study and treatment of particular disease groups under investigation.

As many of you know, the National Institutes of Health comprise six major Institutes—the Experimental Biology and Medicine Institute, the Microbiological Institute, the National Cancer Institute, the National Heart Institute, the National Institute of Dental Research, and the National Institute of Mental Health.

This extensive intramural program is supplemented by a program of research grants and fellowships, which totals many millions of dollars annually. Through these grants, hundreds of universities, hospitals, laboratories and individual scientists throughout the country receive funds to carry on special projects. And through the fellowships, promising young students are enabled to obtain training in their careers as researchers and scientists.

The medical and scientific research program carried on by scientists in Bethesda and at several field stations and laboratories is almost as broad as the attack of disease itself on man.

It extends into practically all fields of medical research and all branches of medical science—not only into cortisone and ACTH, penicillin, aureomycin, the sulfa drugs and other antibiotics, but into heart disease, cancer, mental disease, Rocky Mountain spotted fever, poliomyelitis, brucellosis, Q fever, rabies, typhus, the common cold and scores of other projects which affect the health and welfare of mankind.

Some of these studies are fundamental; others have immediate and direct application. Some seek the nature and cause of specific disease. Others develop drugs, serums, antibiotics, vaccines, or new agents that will aid in the prevention, control or cure of disease.

Working behind their test tubes and microscopes, many of our principal investigators are concerned with problems of chemotherapy and antibiotics, nutrition and metabolism pathology and pharmacology, the nature of cancer, fundamental studies of the diseases of the heart and vascular system. They are studying the general problems associated with the aging process; serology and immunology; electron microscopic study of large molecules, peptic ulcers, and other research to advance human welfare.

### Biologics Control Laboratory

Among our most important activities is the work of the Biologics Control Laboratory which performs functions related to the control of biological products, begun under the Act of Congress of 1902.

I am sure you are all familiar with the regulations for the control of such products—guaranteeing their safety, purity and potency—which are formulated here. You also know of the "dating periods"—the time limit beyond which the product cannot be expected to yield specific results and the conditions of storage during this period—which are also established in this key laboratory.

All firms manufacturing biologic products entering interstate commerce in the United States—regardless of whether they are manufactured here or in a foreign country—must qualify for a license under standards set by the National Institutes of Health.

These licensed laboratories are periodically inspected by staff members of the Biologics Control Laboratory. But because of the splendid cooperation of pharmaceutical manufacturers, pharmacists and physicians, the biologics control law has been administered, rather than enforced. As a result, it has helped this country's great drug industry to produce biologic products that are very highly regarded throughout the world.

This cooperative effort has been tested and proved. It fulfills a vital need. For neither the Federal government nor private organizations can solve these problems alone. The task ahead requires the best efforts of everyone engaged in medical research.

This nation's relative neglect of fundamental research in nearly every field of science must not be allowed to continue. Most of our achievements in the fields of chemotherapy, antibiotics, radiology and atomic fission were made possible by the fundamental discoveries of scientists in other nations. We can no longer afford to rely on the work of others.

Much concern has been expressed recently to the effect that the increased interest of the Federal government in the support of research means government control of research.

Government scientists are the first to agree that authoritative control would defeat the very purpose of government aid. For several years government aid to medical research has gone forward with little or no evidence of the development of such authoritarian methods. The program has been collaborative rather than authoritative. It has added to rather than substituted for privately financed and directed research.

Freedom of investigation is insured in the research grants program of the Public Health Service by the system of National Advisory Health Councils and Study Sections that are established in law or by precedent. They have enlisted the interest and the wisdom of hundreds of this nation's best known leaders in various fields of medical and related research, and of scores of outstanding leaders in public affairs, education, social science, commerce, and voluntary public service.

In making these grants we are guided by a philosophy which guarantees the integrity, independence and freedom from regimentation of the recipient.

The joint effort of government and industry—of public and private health agencies—and of scientists, physicians and pharmacists working together in the common cause has already been demonstrated in the development of penicillin and a score of new drugs.

This same high degree of unselfish cooperation and intensive study will speed the development of ACTH and cortisone as a tool of research—and bring new hope to peoples everywhere.

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## HEALTH INFORMATION FOUNDATION APPOINTEE

**Appointment of Walter E. Boek as chief research analyst of the Health Information Foundation has been announced by Admiral William H. P. Blandy, U.S.N. (Ret.), president of the Foundation.**

**Mr. Boek, who is a graduate of Cornell University and of Michigan State College, where he received his M.A., formerly directed research for the Michigan Agricultural Extension Service in the College's department of sociology and anthropology. He is a member of the American Sociological Society, the Rural Sociological Society, the Society of Applied Anthropology, the American Association for the Advancement of Science and the Michigan Sociological Society.**

# *Ernest G. Eberhardt—A. Ph. A. Honorary President*

ERNEST G. EBERHARDT of Indianapolis Indiana, was elected honorary president of the AMERICAN PHARMACEUTICAL ASSOCIATION for 1950–51 at the Atlantic City Convention.

Mr. Eberhardt, now retired, was the first pharmaceutical chemist employed by Eli Lilly and Company. He joined the company in June, 1886, just after being graduated with honors in Purdue University's first pharmacy class. His first job was testing drugs, assaying samples, and storing narcotics. Although retirement provisions would have permitted Mr. Eberhardt to retire in 1929, he continued as technical adviser at Lilly's until his final retirement in 1948. Through the years, his devotion to his profession was a large part of his exemplary life.

To the JOURNAL'S request for biographical information, Mr. Eberhardt responded with a letter that is alive with his typical keenness and alertness. The following excerpt is quoted from his letter:

*Ernest G. Eberhardt*

"Born in a small village of South Germany, Oct. 15, 1864, I was brought to America by my parents in the spring of 1873, coming directly to Indianapolis where they had some acquaintance. When school days were over, I was employed in a retail drugstore and, after four years' experience, I entered the first class of the new Purdue School of Pharmacy where the training given was also first class. After graduating with honors in the spring of 1886, I was employed as chemist by Eli Lilly and Company in that same year.

"In 1889 I was given a year's leave of absence for special studies in plant analysis at the Philadelphia College of Pharmacy under Professor Trimble. As a special student I had the privilege of attending the regular lectures, which I did, for those were the days of Maisch, Remington and Sadtler. At the end of the school year I was induced to take the final examinations, thus becoming an alumnus of that historic institution. Since then I have served Eli Lilly and Company in various capacities until the time of retirement in 1945, but by special permission continued work until final retirement in 1948.

"Shortly after my return from Philadelphia to Indianapolis, I was married to a fine young lady of the First Evangelical Church of that city; I joined her in church membership as well as in faith. She was an ideal wife and mother of two sons and four daughters. She went to her reward in 1929, leaving her children grown and all but one married. All are still living and, in addition, I have 13 grandchildren and two great-grandchildren. I have been a member of my church (New York St. Evangelical United Brethren) for more than 60 years and am now trustee-emeritus. I find no difficulty in maintaining an interest in life, but because of the handicaps of old age I find there is no place like home for both the present and the future. The three things which have mainly claimed my interest are my home, my job, and my church."

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## "MASTER OF DRUGS"

Under this caption, the Maryland State Board of Health of which Dr. E. F. Kelly, Secretary of the AMERICAN PHARMACEUTICAL ASSOCIATION from 1925 to 1944, was a member for many years, recorded the following resolution:

"The establishment of a Kelly Memorial building as described by Geoffrey W. Fielding in the *Baltimore Sun* of Sunday morning, October 9, 1949, pleased the Maryland State Board of Health beyond measure.

"The erection of this memorial to Dr. Evander F. Kelly by a group representing the AMERICAN PHARMACEUTICAL ASSOCIATION and the Maryland Pharmaceutical Association is one of the finest things that could be done.

"If ever there was a more lovable, a more self-effacing, or a more capable man in his particular line, we fail to remember who he was. Kelly was beloved by all members of the State Board of Health and his passing was a keen loss to each and all of us.

"How appropriate that the meetings of the Pharmaceutical Association are to be held in this memorial building. It will be a constant reminder of a beloved man—a man who did so much for his profession."

Members of the AMERICAN PHARMACEUTICAL ASSOCIATION and other readers of THIS JOURNAL may send their contributions to the Kelly Memorial to Dr. H. A. B. Dunning, General Chairman of the Committee, Charles and Chase Streets, Baltimore, Md.

# The 1950 National Formulary

by Justin L. Powers

Chairman, Committee on National Formulary, American Pharmaceutical Association

THE NEW ninth edition of the National Formulary will be published and ready for distribution at about the time the July issue of THIS JOURNAL is released. This edition of the National Formulary is the third to be published under a plan adopted by the Council of the AMERICAN PHARMACEUTICAL ASSOCIATION in 1938 for the publication and revision of the National Formulary at five-year instead of ten-year intervals. The date on which the requirements of N. F. IX become official is November 1, 1950.

During the course of the revision of N. F. VIII leading to the publication of the ninth edition, many extensive and significant changes in the content of the text were made. A fairly high proportion of the monographs on drugs and dosage forms appearing in the eighth edition has been continued in the ninth. A total of 162 items official in N. F. VIII were not admitted to N. F. IX. A complete list of these titles (1) has already been published and that list with but few exceptions is correct.

Titles and standards for 155 drugs for which official standards would not otherwise be provided have been added to N. F. IX during the recently completed revision program. A high proportion of these provide official specifications for many widely used drugs not previously included in either the United States Pharmacopeia or the National Formulary. Among the new admissions are such drugs and preparations as amobarbital (Amytal) and dosage forms, anthralin ointment, camphorated parachlorophenol, dehydrocholic acid, glutamic acid hydrochloride, liver products for oral use, racephedrine hydrochloride capsules and solution, rutin and rutin tablets, and undecylenic acid and ointment. In addition formulas and standards are continued in the National Formulary for many U. S. P. XIII drugs not admitted to U. S. P. XIV, of which alum, citrated caffeine, chalk

mixture, chloroform liniment, compound effervescent powders, mercurous chloride, potassium arsenite solution, potassium sodium tartrate, rhubarb and its preparations, senna and its preparations, and thymol are a few typical examples.

In the process of revision many individual specifications for strength, quality, purity and identity for previously official drugs have been thoroughly revised and materially improved. Several new features have also been added. Among these are specifications for the disintegration time of tablets, weight variation standards for tablets and for the contents of dry-filled ampuls and other containers.

### N. F. IX Scope

The general principles followed by the Committee on National Formulary in the compilation of the ninth edition have not been materially changed from previous editions. The purpose continues to be the establishment and promulgation of official standards for drugs. The admission of drugs to this edition has, as in the past, been based not only on therapeutic value but also upon the extent of use. The extent of use of certain N. F. drugs was determined, in part, by a survey (2) conducted early in 1948. This survey was designed to determine what N. F. VIII drugs had become obsolete and were no longer being prescribed by physicians or dispensed by pharmacists other than on prescriptions. It involved the mailing of check lists to nearly 1000 statistically selected pharmacies. The response to this request, from the pharmacists whose cooperation was sought, was excellent. Between 30 and 40 per cent of the check lists mailed were returned. The assistance furnished by the practicing pharmacists who were requested to supply the Committee on National Formulary with certain information was of great help in reaching final decisions on deletions.

### The Significance and Function of the N. F.

Changing conditions and needs of a profession require corresponding changes in the nature of the information which serves the profession. Thus the National Formulary has been undergoing changes continually since the appearance of the first edition in 1888. In the beginning the National Formulary served only as a convenience to practicing pharmacists by providing uniform names, uniform formulas, and working directions for the small-scale manufacturer of pharmaceutical preparations frequently prescribed by physicians. Until 1906, when it was designated as one of the two official compendia by the terms of the Federal Food and Drug Law, the function and significance of the National Formulary remained practically unchanged.

The provisions of the 1906 law and the Federal Food, Drug and Cosmetic Act of 1938, however, increased the obligation of the AMERICN PHARMACEUTICAL ASSOCIATION in the revision of the National Formulary and added greatly to its significance. Today the National Formulary renders a distinct service to pharmacists and pharmaceutical manufacturers by providing specifications for the procurement of drugs used in dispensing, prescription compounding, and manufacturing, in addition to providing formulas and working directions for the preparation of dosage forms. It provides standards for use by state and federal Food and Drug Administration officials in their enforcement programs, and thus simplifies their procedures. The activities and functions of the National Formulary add up to a distinctive and important pharmaceutical service to the public.

The position of the National Formulary as a book of legal standards for drugs is made clear by a consideration of the authority conferred upon it by the 1938 Federal Food, Drug, and Cosmetic Act. Section 501(c) of this statute requires that drugs purporting to be those listed in the National Formulary must conform to the standards of strength, quality, purity, and identity prescribed by that compendium. All determinations of these standards must be made in accordance with the methods described in the text. Variations from these standards are permitted only when certain labeling requirements of the Act are met.

The same section of the Act confers authority upon the Administrator to prescribe tests where none have been provided or where those described are, in his opinion, insufficient. Before the Administrator can take such action, however, he must first call to the attention of those responsible for the revision of the National Formulary the

need for additional or more adequate tests. He may then proceed only after a reasonable time has elapsed, and the revision committee has failed to provide adequate tests or methods of assay. Thus, while considerable authority to promulgate standards is conferred by the Act upon the AMERICAN PHARMACEUTICAL ASSOCIATION and its Committee on National Formulary, adequate checks and safeguards against arbitrary or scientifically unsound specifications are also provided.

The AMERICAN PHARMACEUTICAL ASSOCIATION'S National Formulary revision program for the past ten years has been on a continuous revision basis. It will continue on that basis. Tentative plans have already been formulated for the beginning of another five-year program as soon as the ninth edition is completed. It is the expectation of the Committee on National Formulary that a program, even more aggressive and progressive than those of the past, may be planned and carried to completion in the next five-year period culminating in the publication of the tenth edition of the National Formulary in 1955.

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## SIXTH INSTITUTE ON HOSPITAL PHARMACY

WITH a record attendance of 154 registrants, the Sixth Institute on Hospital Pharmacy was held on the campus of University of Michigan in Ann Arbor, during the week of June 19. The Division of Hospital Pharmacy of the AMERICAN PHARMACEUTICAL ASSOCIATION and the American Society of Hospital Pharmacists again cooperated with the American Hospital Association in making this educational meeting for hospital pharmacists possible. Hospitals of all sizes and types were represented offering an opportunity for exchange of ideas among the participants.

### *Five-day Session*

Four principal themes covered during the five-day session included: Hospital Pharmacy Organization; Hospital Pharmacy Administration; Pharmaceutical Aspects of Production and Utilization of Currently Important Drugs; and Current Trends in Pharmacology and Therapeutics. Included on the program were lectures by outstanding hospital pharmacists as well as representatives from the allied health fields. Supplementing the lectures were demonstrations, panel discussions and a work shop on problems in hospital pharmacy. Those attending the Institute were also given an opportunity to tour the pharmacy department at the University of Michigan Hospital.

### *Organization and Administration*

Under hospital pharmacy organization, subjects covered included: Fundamental Principles of Organization and Administration; Principles of Departmental Organization and Administration within the Hospital; Expanding Pharmacy Service in the Hospital; and the Attitude and Responsibility of the Pharmacist as a Member of the Medical Team.

Highlighting the discussions on hospital pharmacy administration was a presentation of the revised Suggested Floor Plans for Pharmacies in Hospitals as prepared by the Hospital Facilities Division of the Public Health Service in cooperation with the Division of Hospital Pharmacy. Discussing the elements of planning a new pharmacy department or pharmacy expansion, Dr. John R. McGibony, Medical Director, Chief, Division of Medical and Hospital Resources, Public Health Service, presented the plans along with suggestions for future expansion. Included also under hospital pharmacy administration were discussions on business records for the pharmacy, prescription charges and development of a therapeutics committee.

### *New Drugs*

One day was devoted to discussion of the pharmacology and therapeutics of the newer drugs including: the autonomic drugs; the cardiac drugs; drugs used in anemia and related blood disorders; drugs used in the treatment of arthritis; evaluation of the antihistamine drugs; and discussion of the present status of antibiotics.

Methods for the production and utilization of currently important drugs, including the sulfonamides, eye solutions, antibiotics, and vitamin-preparations, were outlined.

### *Work Shop*

An outstanding event in the week's program was the work shop on hospital pharmacy problems. Topics discussed included: After Hours and Emergency Requests for Drugs; Narcotic Control Methods; Refilling of Prescriptions; Teaching Pharmacology to Nurses; Extra-Pharmaceutical Services; Who Shall Do the Purchasing for the Pharmacy; and When Is It Possible to Manufacture. Leaders of each of the groups presented a summary of the decisions reached in each of the discussions.

Closing the meeting on Friday night with a banquet, Dr. A. C. Kerlikowske, administrator at University Hospital, awarded the certificates on behalf of the sponsoring organizations.

# Pharmacists Receive Army Reserve Commissions

The four colleges of pharmacy selected in 1948 as pioneers in the development of a Pharmacy ROTC Program—the Universities of California, Ohio State, Minnesota, and Wisconsin—have graduated their first students completing the program.

The University of California awarded degrees in Pharmacy to nineteen graduates who also received commissions as Second Lieutenants in the Army's Reserve Medical Service Corps.

It is anticipated that this experiment in the training of pharmacists for the military reserve will be continued and that other institutions will be included in the training program as the fiscal and military policies of the Government permit. In many institutions pharmacy students may join the ROTC for military training but not in separate units for students in the medical and auxiliary professional groups.

It will be recalled that THIS JOURNAL announced the development of ROTC training in professional groups related to medicine. It was hoped that training in such a unit for prospective physicians, dentists, pharmacists, and other health personnel would emphasize, at an early stage in the preparation for a military career, the importance of team work in developing the medical program of the Armed Forces.

*University of California Commissioned Pharmacists—Left to right: (front row) Maj. Woodrow C. Herbert, MSC; Louie Woon; William C. Demele, class president; Dr. Troy C. Daniels, Dean of the College of Pharmacy; Andrew A. Wong; Allan T. Benko; M/Sgt. John H. Arthur, asst. to Maj. Herbert. (middle row) Donald J. Benedetti; Russell C. Hausman; Charles E. Jackson; Ralph A. Dreike; George L. Harder; Leland J. Harris; and Frank E. Zaballos. (back row) Benjamin E. Schnereger; James G. Moore; John F. Cunningham; Richard L. Less; Stanley M. Viscia; William G. Brierly; and James F. Green. (Note: Lloyd R. Daniels, another member of the class, was not present for the photograph.)*

## CHIEF OF FDA NEW DRUG SECTION APPOINTED

The appointment of Dr. Ralph Grafton Smith as Chief of the New Drug Section of the Division of Medicine, Food and Drug Administration, was announced June 3. Dr. Smith was formerly professor and chairman of the Department of Pharmacology at Tulane University School of Medicine in New Orleans. His appointment is considered a key assignment in the Food and Drug Administration because the Chief of the New Drug Section is responsible for evaluating the safety of every new drug before it is permitted to be placed on the market.

In commenting on the new appointment, Dr. Paul B. Dunbar, Commissioner of Food and Drugs, explained that with their applications for the introduction of new drugs, the manufacturers submit scientific proof that the drug will be safe for the consumer if used according to the directions specified in the labeling. The Chief of the New Drug Section must determine whether the tests the manufacturers have made are adequate to assure the protection of the health of the American public. With the tremendous strides in the development of new drugs since Congress enacted this safety provision in 1938, the responsibility of admitting valuable new drugs, and at the same time delaying their use until the potential danger of untried drugs is forestalled, must be entrusted to scientists with expert knowledge of both medicine and pharmacology.

Dr. Dunbar said that Dr. Smith was recommended as his successor by Dr. Erwin E. Nelson, when the latter relinquished his assignment as New Drug Chief, to become Medical Director of the Food and Drug Administration in January, 1950. He pointed out that Dr. Smith brings to this important position an impressive background of training and experience.

# Rationale for the use of Ovarian and Testicular Hormones in Human Therapy

*by L. Earle Arnow, M.D.**

SCATTERED throughout the body are isolated groups of cells called endocrine, or ductless glands, which manufacture the substances called hormones. As their name implies, ductless glands do not have ducts, and hormones pass directly from the cells that manufacture them into the blood stream. It is generally true that hormones do not affect the cells that make them; instead they are carried by the blood to some other organ or tissue, where they produce their characteristic effects. Most hormones are stimulating substances, and the term, hormone, is derived from a Greek word meaning "to stimulate."

### Hormones of the Ovary

In a normal menstrual cycle, shortly before expulsion, the ovum is located in a hollow space called a follicle which is filled with follicular fluid and lined by cells called follicle cells. At ovulation, the follicle ruptures and the ovum is expelled into the body cavity. The follicle then fills with a blood clot, which is replaced in a few days by large cells that have a yellow color. This mass of cells is called the corpus luteum (yellow body). If pregnancy does not occur, the corpus luteum soon is replaced by scar tissue; but if the ovum is fertilized, the corpus luteum remains for the first three or four months of pregnancy.

The hormone made by the follicle cells is called estradiol. Apparently this substance can be changed chemically in the body into other substances that are eliminated in the urine. Estrone and estriol are the most important of these. All of these substances exhibit hormonal activity when they are injected into animals, and they are known collectively as the follicular or estrogenic hormones.

During menstruation, the lining of the uterus (the endometrium) largely sloughs off and is expelled with the menstrual blood. The regeneration of the endometrium that begins after menstruation is caused by the follicular hormones. At about the fourteenth day of the menstrual cycle the follicle ruptures and the ovum is expelled. At this time the endometrium is much thicker, and the excretion of follicular hormones in the urine has risen to a peak. Following the rupture of the follicle, the excretion of these hormones rapidly falls. A second rise occurs before the beginning of the next menstrual period. Presumably this secondary rise results from the production of estrogenic hormones by the corpus luteum.

Changes in the endometrium that occur during the second half of the menstrual cycle are caused mainly by progesterone, a hormone secreted by the corpus luteum cells. Progesterone causes an engorgement of the endometrium with blood and, under its influence, the endometrial glands fill with secretion. A certain type of cell, which is used to help form the placenta if pregnancy occurs, develops as a result of progesterone stimulation. In other words, progesterone appears to prepare the endometrium for the nourishment and attachment of the fertilized ovum. If the ovum is not fertilized, the production of both progesterone and estrogens ceases rather abruptly on about the twenty-third or twenty-fourth day of the menstrual cycle; menstruation follows in four or five days. This sudden failure on the part of the ovary to manufacture its hormones is thought to be responsible for the appearance of menstruation.

Progesterone and estrogens are secreted throughout pregnancy. For a time they are

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made by the corpus luteum, but later in pregnancy the placenta manufactures them.

Cyclic changes also take place in the lining of the vagina and are caused by the estrogens. The estrogens, progesterone, and a pituitary hormone appear to be responsible for the growth of the mammary glands at the time of menstruation and during pregnancy.

Progesterone is changed in the body to a compound called pregnanediol. Pregnanediol unites with sodium and glycuronic acid (an organic acid related chemically to glucose) and then is excreted in the urine. It is an interesting finding that estrogens occur in the urine of both females and males. Indeed, one of the best sources of these hormones is the urine of the stallion. Pregnancy urine also is an excellent source.

### Hormones of the Testis

The male sex hormone testosterone is manufactured by the interstitial cells of the testis and apparently is changed in the body to other substances that also have hormone activity. The most important of these is androsterone. So far, testosterone has been obtained only from the testis itself, and androsterone has been isolated only from urine. This causes us to suppose that testosterone is manufactured in the interstitial cells and is later converted to androsterone, which is excreted in the urine. Some testosterone probably is converted to substances other than androsterone.

### Experimental Production of Uterine Bleeding

If the estrogens are administered in sufficiently large doses for a sufficiently long period of time, bleeding from the endometrium (lining of the uterus) will occur. Probably estrogens cause an increase in the thickness of the endometrium to a point where the outer layers slough off; this is the cause of the bleeding.

Another type of uterine bleeding can be produced by the sudden withdrawal of estrogen following its administration for a time. In other words, if the physician gives a sufficiently large dosage of estrogen for a time and then suddenly ceases giving it to the patient, in about seven to ten days the estrogen-primed endometrium of the uterus will slough off and bleeding will occur for a period of three or four days.

If there is a normal endometrium in the uterus (that is, if the patient has circulating within her tissues sufficient estrogen to allow some thickening of the endometrium) bleeding can be induced also by giving progesterone for a period of time and then ceasing its administration. This is referred to as progesterone withdrawal bleeding.

### Anovulatory Cycles

As we have seen, in a normal menstrual cycle, the follicle ruptures (i.e., ovulation occurs) at about the midpoint, after which the corpus luteum forms. During the first few menstrual cycles that appear during adolescence, however, this follicle, although it may grow and produce estrogens, does not rupture so that no corpus luteum is formed. Under such circumstances, of course, no progesterone is formed. There may be bleeding, which is interpreted by the individual as normal menstrual bleeding, because of the sudden drop of circulating estrogens toward the end of the menstrual period. In other words, the bleeding is due to estrogen withdrawal. Sometimes older women likewise have cycles that are anovulatory. It is important to remember this in order to understand some of the clinical indications for the use of estrogens.

### Pituitary Control of the Ovary

One part of the pituitary, known as the anterior lobe, secretes several important hormones. Three of these are of interest in connection with the present discussion. One of them, known as the follicle-stimulating hormone, or FSH, is responsible for the growth of the follicle and for production of the estrogens by the cells that line the follicle. This hormone is produced in constantly increasing amounts throughout the first half of the menstrual cycle. When, however, the estrogen level in the blood reaches a certain point, this inhibits the secretion of FSH and is the explanation of the drop in estrogen production that occurs near the midpoint of the cycle. Following this drop in circulating estrogens, FSH production begins again and, as already stated, there is a secondary rise in estrogen production during the latter half of the cycle. Toward the end of the cycle, the estrogen level again is high enough to inhibit FSH production with a resulting fall in estrogen level. In the male, FSH is required for the development of the spermatozoa.

Another important pituitary hormone is known as the luteinizing hormone or LH. This hormone, together with FSH, appears to cause the actual ovulation or expulsion of the egg from the follicle. Moreover, it probably initiates the growth of the corpus luteum. Peak production of LH by the pituitary occurs shortly before the midpoint of the menstrual cycle. In the male, LH stimulates the interstitial cells that manufacture male sex hormones.

The third pituitary hormone that has an important effect on the ovary is known variously as prolactin, lactogenic hormone, or luteotrophic hormone. This hormone is required for the maintenance and growth of the corpus luteum and hence for the production of progesterone. It is secreted during the latter half of the menstrual cycle. Incidentally, it appears to be responsible also for the initiation of milk production by the mammary gland following childbirth.

### Clinical Indications for the Use of Estrogens and Progesterone

*Management of the Abnormal Menopause.* Approximately one-third of the women who go through the menopause have sufficiently distressing symptoms to seek medical aid. When the ovary ceases production of estrogens, the pituitary gland then produces very large amounts of FSH. Although the cause of the signs and symptoms of the abnormal menopause is not known with certainty, many clinicians believe that they may be due to the excessive production of this hormone. When estrogens are given, the pituitary is inhibited and hence makes less FSH. This is the usually accepted rationale for giving estrogens for this condition and the great majority of women obtain prompt relief.

*Hypo-ovarianism.* This condition is assumed to be present when the signs of estrogen production (such as breast development, appearance of pubic hair, onset of the menses) are absent in a woman or girl of adult age. The administration of estrogens will cause this preadolescent type of individual to become adult in appearance and mental reactions. In many cases, the patient's own ovary eventually will take over and produce estrogens. In other cases, the physican may have to use estrogens or a combination of estrogens and progesterone for a long time in order to maintain the individual in an adult state.

*Amenorrhea.* This condition is said to be primary if the patient never has had a menstrual period and secondary if the menstrual periods cease after they have been initiated. The usual cause of primary amenorrhea is hypo-ovarianism as described above. Occasionally, however, it may be due to the presence of anovulatory cycles accompanied by insufficient estrogen production so that withdrawal bleeding does not occur. In older women who previously have had normal menstrual cycles, amenorrhea may be caused by pregnancy or by some abnormal condition such as the presence of a tumor or infection. If these obvious causes are ruled out by careful diagnostic procedures, the remaining usual cause is again the occurrence of a persistent anovulatory cycle. This may be remedied by the administration of estrogens, progesterone, or both for a period of time so that withdrawal bleeding will occur. Following this bleeding, frequently normal menstrual cycles then will appear, although in some cases it may be necessary to repeat therapy for many months.

*Functional Uterine Bleeding* This term is used to refer to any type of abnormal uterine bleeding that cannot be explained by the presence of tumors, infections, or other obvious conditions. The usual cause of functional uterine bleeding again is the occurrence of anovulatory cycles. If, during this anovulatory cycle, a sufficient quantity of estrogen is produced, uterine bleeding will take place. This will occur either constantly if the estrogen production is maintained at a high level or intermittently if the production of estrogens varies at different periods of time. Estrogens and progesterone, or combinations of both, can be employed to cause withdrawal bleeding and hence the initiation of a new menstrual cycle. Frequently, this will cause resumption of normal periods without abnormal bleeding.

*Dysmenorrhea.* If estrogens are employed to combat dysmenorrhea, they are given in high dosages during the first half of the cycle. This inhibits production of FSH and suppresses ovulation. After therapy is discontinued, painless estrogen withdrawal bleeding (interpreted by the patient as a normal menstrual period) occurs. Another method of treatment consists in giving progesterone during the last two or three days of the menstrual cycle, using rather small doses. Experimentally, it has been noted that pro-

gesterone withdrawal bleeding (which occurs usually within two or three days after ceasing to administer progesterone) is accompanied by cramping pains resembling dysmenorrhea. The idea of the small doses is to prevent a sudden drop in the progesterone level since, experimentally, this will cause dysmenorrhea.

*Vaginitis.* In children and in women who do not manufacture estrogens, the lining of the vagina is rather thin and has a pH close to neutrality. Under the influence of estrogens, the lining thickens considerably, stores relatively large amounts of glycogen, and produces lactic and other acids. This gives a marked fall in pH so that the vaginal secretions of normal adult estrogen-producing women is 4.5 or lower. Vaginal infections, such as gonorrhea in young girls, can be treated by the administration of estrogens either in the usual way or in the form of suppositories. This causes the lining of the vagina to become adult in type and the resulting low pH makes bacterial growth difficult or even impossible. This same type of therapy is useful in treating any type of vaginitis regardless of the age of the patient.

*Breast diseases.* (a) Hypomastia (underdeveloped breasts). The development of the breast tissue at the time of puberty is caused primarily by estrogen stimulation. Enlargement of the breasts therefore can be caused by administration of estrogens either in the usual way or by direct application of ointments to the breast area. This procedure is not employed widely, however, since when therapy is terminated, the breasts usually shrink in size again.

(b) Painful engorgement of lactating breasts. During the nursing period, the administration of large doses of estrogen does not inhibit lactation. If, however, for some reason nursing is terminated, the resulting painful engorgement that may continue for some days can be relieved by giving estrogens (or, as discussed later, androgens) in very high doses. Presumably this procedure inhibits the pituitary so that its hormones cease to act on the breast.

(c) Cancer in post-menopausal women. In older women who have breast cancer, there sometimes are metastases (secondary cancer growths that have originated from the primary one) located in various soft tissues throughout the body. These metastases often are very painful. It has been found that administration of large doses of estrogens may, in some cases, relieve the pain although, of course, it will not cure the cancer.

*Abortion.* The term habitual abortion refers to the case in which the woman has had several abortions so that the chances of her having one during her present pregnancy are rather high. Threatened abortion means that some sign, such as vaginal bleeding, has caused the physician to suspect that the patient is in danger of having an abortion sometime during pregnancy. As we have noted already, in the event of pregnancy, the corpus luteum persists and large amounts of estrogens and progesterone are produced. This production of hormones continues at an increasing rate until just prior to pregnancy, when there is a sudden drop in production of both hormones. It appears that most of this excess hormone production takes place not in the ovary but rather in the placenta. There is good evidence, also, that the placenta begins to make its ovarian-type hormones at about the third month of pregnancy. Now the corpus luteum, and possibly the other structures in the ovary, frequently atrophy at about the third month and cease hormone production. In a normal situation, this loss of ovarian function is unimportant since the placenta carries on. If, however, placental hormone production is not yet well established, abortion may occur as a result of the failure of estrogen and progesterone formation. It is a common clinical observation that most abortions do occur at the third month of pregnancy.

In the case of habitual abortion, therefore, it is common practice to give large doses of progesterone to the patient throughout the first half, at least, of the pregnancy. Recently, evidence has accumulated indicating that it may be wise also to give large doses of estrogens during this time. In the event that there is evidence of a threatened abortion, most physicians start hormone therapy at once using large doses of progesterone. Again, some physicians now use also large doses of estrogens. Threatened abortion may occur at any time during the pregnancy and therapy usually is continued until the expected date of delivery.

*Prostate Diseases.* Elderly males frequently have an enlargement of this gland with resultant difficulty in urination. This may be a simple enlargement (known as benign hypertrophy), or, much less commonly,

it may be an enlargement due to cancer of the prostate. Some years ago Doctor Huggins at the University of Chicago discovered that the removal of the testes of men with cancer of the prostate caused some loss in size of the cancer tumor and also gave rather dramatic relief of pain. He tried this procedure since it was known that the male sex hormones will stimulate the growth of prostate tissue. He felt, therefore, that removal of this hormone might be beneficial. This proved to be the case. Following this same line of reasoning, other people have used estrogens. This was done since estrogens are known to cause atrophy of the epithelium of the prostate in laboratory animals. It is now known that large doses of estrogen produce results that are comparable with those obtained by removal of the testes. In other words, cancer is not cured but pain is relieved and the patient probably lives several years longer than would have been the case without therapy.

*Premenstrual Tension.* Some women, prior to menstruation, experience an annoying group of signs and symptoms. Among these are edema (abnormal collection of fluid in the tissues) with resulting swollen ankles and general puffiness, nervousness, emotional instability, and perhaps headache. Experimentally it has been found that estrogens cause a retention of water by animals and it has been presumed that excess estrogen production may be the cause of premenstrual tension in women. In any case, whatever the cause, the administration of progesterone during the last half of the cycle often will relieve the symptoms. Apparently progesterone antagonizes some of the physiological effects of estrogens.

### Clinical Indications for the Use of Androgens

***In the Male:***

*Male Climacteric.* It has become evident in recent years that a certain number of men undergo a failure of male sex hormone production at ages roughly comparable to the menopausal age in women. Many clinicians regard this so-called "male climacteric" as a definite clinical entity although this still is controversial. These people have symptoms of fatigue, hot flushes, childish behavior, and nervousness. Apparently, many such individuals can be treated successfully with androgens. This is, of course, replacement therapy and usually has to be continued for a considerable period of time.

*Eunuchism (Hypogonadism).* This is a condition in which the testis fails to produce sufficient hormone at and following puberty. There is, therefore, a failure of development of secondary sex characteristics. The use of male sex hormones in the therapy of this condition is obvious. Therapy may have to be continued throughout the individual's life.

*Impotence.* Loss of sexual potency may be due to a failure on the part of the patient to produce sufficient male sex hormones. Frequently this condition can be remedied by the use of these hormones although usually psychiatric assistance is required also.

*Cryptorchidism (Undescended Testis).* At a time prior to birth, the two testes are located in the abdominal cavity. Ordinarily, shortly before birth they descend into the scrotum. Occasionally, however, one or both of them fails to descend at birth. A certain percentage of these abnormally located testes will descend into the scrotum at puberty. Presumably, this is caused by the increase in size of the testes which takes place as a result of stimulation by sex hormones. This increase in size forces the structure down into the scrotum. Partly for cosmetic reasons and partly because a testis located in the abdominal cavity does not produce viable sperm or normal amounts of hormone (this is caused by the slightly higher temperature of the abdominal cavity as contrasted to that of the testis) it is desirable to cause descent into the scrotum at or before puberty. If there is some type of mechanical obstruction, this can be done only by surgery. However, a small but definite percentage of good clinical results can be obtained by the cautious use of androgens. It is more common today to use chorionic gonadotropin (a hormone obtained from the urine of pregnant women) which stimulates the production of androgens in the patient's own body.

***In the Female:***

In most cases, the rationale for the use of male hormones in the case of females can be explained by assuming that this type of hormone can suppress pituitary function. This,

in turn, decreases the production of estrogens by the ovary. It should be remembered that if an amount of androgen equivalent to 500 mg. or more of testosterone propionate (administered parenterally) is given within the period of a month to the average woman, signs of overdosage will appear. (It should be appreciated that this figure is only approximate and will vary from patient to patient.) Thus there may be some appearance of hair on the face, the voice may deepen, menses will stop, and acne may appear.

*Breast Diseases.* (a) Cancer. Metastases from cancer of the breast frequently localize in bones. Recent studies have indicated that massive doses of androgens frequently will cause a bone metastasis to disappear and will give dramatic relief of pain. This is in no sense a cure of the cancer but it does give relief and actually may increase the life span of the patients by several years.

(b) Painful engorgement during lactation. The androgens, like estrogens, will not inhibit lactation in the nursing breast. However, if the mother is not nursing her baby, painful engorgement of the breast can be relieved by the use of male hormones (as well as, of course, by the use of estrogens). The reason for the effectiveness of androgens is not known although it is possible that it may act by inhibiting the production of hormones by the pituitary.

*Dysmenorrhea.* In some instances, androgens have been used effectively to prevent dysmenorrhea. Some people have guessed that the chemical similarity of testosterone to progesterone may make it possible for testosterone to diminish the effects of a sudden progesterone withdrawal. It will be recalled that progesterone is effective in many cases of dysmenorrhea presumably because administering it prevents a sudden lack of this material from the body. It may be that testosterone is enough like progesterone to substitute for it, at least in part.

*Menopause.* Obviously an estrogen is the drug of choice for the treatment of the abnormal menopause. However, in occasional women, this type of hormone is unsatisfactory because it produces tension states, engorged breasts, excessive bleeding, or other undesirable conditions. If this occurs, androgens can be used and act, presumably, by suppressing the secretion of FSH by the pituitary.

*Functional Uterine Bleeding.* As stated above, it is believed that the commonest cause of functional uterine bleeding is the anovulatory cycle. The bleeding, of course, is due to excessive estrogen production. Testosterone frequently will control this condition, presumably by decreasing the production of estrogen by the patient's ovary. This result is brought about again by an inhibition of the anterior pituitary gland.

*Premenstrual Tension.* As mentioned under the discussion on estrogen, the phenomenon causing premenstrual tension is believed to be the excessive production of estrogen. It is not surprising, therefore, that testosterone is effective in many cases in controlling this condition since it will decrease the patient's production of estrogen.

### Contraindications for the Use of Androgens

(1) Androgens should never be given to patients with carcinoma of the prostate since there is good reason to believe that this procedure may increase the rapidity of growth of the tumor.

(2) It has been found that androgens result in the retention of sodium and of water; hence they should not be used in the presence of clinical edema (dropsy) since probably they will increase the extent of this edema.

(3) Some clinical investigators have feared that testicular damage might result from giving androgens over long periods of time to individuals with normal testes. In other words, they have pointed out that androgens given in large doses inhibit the anterior pituitary with the result that the cells in the testes that make sex hormones are inhibited. To put it another way, the so-called interstitial cells of the testes, which make male sex hormones, do so only when they are stimulated by LH from the anterior pituitary. Also, probably as a result of a lack of pituitary hormones, testes do not form spermatozoa during periods when large doses of androgens are being given to the patient. However, this result is only temporary and the testes regain their power to produce sperm cells rapidly after therapy is discontinued. It should be appreciated that testosterone does not inhibit spermatogenesis unless massive doses are given. Probably small doses, theoretically at least, actually should stimulate formation of spermatozoa.

# SURVEY FINDINGS ANALYZED

***. . . a review of the findings and recommendations of the Pharmaceutical Survey for the practicing pharmacist . . . . . .***

## THE FINANCING OF PHARMACEUTICAL EDUCATION

THIS article, the ninth of a series on the "Findings and Recommendations of the Pharmaceutical Survey" deals with the problem of the financing of pharmaceutical education.

### Twofold Problem

The Survey presented the financing of pharmaceutical education as a twofold problem. First, that of developing energetic activity by local pharmaceutical interests to present to public authorities the financial needs of institutions supported by public funds. Second, that of securing a concerted willingness on the part of the whole of the pharmaceutical industry and those whose products are distributed through retail drugstores to assume a rightful share of the responsibility for the financial welfare of the colleges and schools.

### Higher Compensation for Teaching Staffs

The Survey found the needs of the colleges and schools of pharmacy to be especially critical as to the compensation of the teaching staffs. "The General Report of the Pharmaceutical Survey," published subsequent to the issuance of the "Findings and Recommendations of the Pharmaceutical Survey," illustrates this point with a chart on the annual salaries of the teaching staffs of sixty-three accredited colleges of pharmacy for the year 1947–48. Half of the deans received salaries below $6500; approximately one-half of the full-time professors received less than $5000; a little over one-half of the full-time associate professors received less than $4500; approximately one-half of the associate professors received less than $4000; and 62 per cent of the full-time instructors received less than $3000. It was the viewpoint of the Survey Committee that adequate compensation for the teaching staff is essential if the profession is to maintain itself on a high level.

### Per-Student Costs

The Survey calculated an annual per-student cost in the accredited colleges and schools of pharmacy on the basis of the amount expended for salaries of full-time teaching staffs in the professional departments of pharmacy, pharmacology, pharmacognosy, pharmaceutical chemistry, and pharmaceutical economics. This revealed the average annual per-student faculty salary to be $101, with the median salary of $90. The highest was $288 and the lowest $30.

### Physical Facility and Equipment Needs

"The General Report of the Pharmaceutical Survey" reveals that in 1948–49, forty-three accredited institutions reported needs for physical facilities totaling $27,033,-500 (based on prevailing costs). Thirteen institutions reported no such expenditures required and seven institutions either replied indefinitely or gave no estimates. As to equipment needs, thirty-five institutions reported pressing needs for equipment estimated to cost somewhat more than $2,500,000. Twenty-nine institutions reported no expenditures necessary for equipment beyond provisions already made.

### Is Pharmacy Getting Its Rightful Share

The Survey took note of the fact that during recent years the leading manufacturers and distributors of pharmaceutical products have provided considerable financial assistance to institutions devoted to medical education and research. They pointed out that the creation and operation of the American Foundation for Pharmaceutical Education is convincing evidence that these same representatives of pharmaceutical industry and commerce have not neglected to include pharmacy within the range of their helpfulness. Nevertheless, in noting the amount of the grants made during the past five years to medicine as compared with the grants made to phar-

macy, the Survey raised the question as to whether pharmacy has been the recipient of its rightful proportion of such grants.

### Recommendations

The Survey directed two recommendations to meet the twofold problem which it set forth.

1. It recommended that carefully planned efforts be made to cause the administrative authorities of each educational institution to know and to understand the financial needs of its college or school of pharmacy.

2. It recommended that the individual establishments comprising the *business* of pharmacy recognize and assume their direct professional and financial responsibility for the effective maintenance of the *profession* of pharmacy through the support of pharmaceutical education.

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## HOSPITAL SERVICE IN THE UNITED STATES

Hospitals registered by the American Medical Association in 1949 increased from 6335 to 6572, according to the annual hospital report of the A. M. A. Council on Medical Education in Hospitals, published in the May 7 issue of the *Journal* of the A. M. A. Included in this group are many of the hospitals recently completed under the National Hospital Program, which to date has authorized more than 1000 projects.

Statistics showed that the number of patients admitted in the various types of hospitals increased from 10,087,548 in 1940 to 16,659,973 in 1949. Bed capacity in 1949 was 1,439,030; 1,226,245 in 1940.

Non-government hospitals furnished the main portion of hospital service. In 1949, of the total patients admitted, 12,401,158 were in non-government hospitals, while 4,258,785 were in hospitals operated by federal, state or local governments.

Hospitals operated by non-profit associations cared for more patients during 1949 than hospitals administered by any other type of agency. These include the church related hospitals with 4,758,922 admissions, and other non-profit association hospitals with 6,089,085. Proprietary hospitals ranked second with 1,553,111 admissions. Federal and city hospitals ranked third and fourth with 1,190,285 and 1,164,096 admissions, respectively.

Classification by types of institutions shows that 40 per cent of the beds were distributed in general hospitals, 49 per cent in psychiatric institutions, 5.8 per cent in tuberculosis sanitariums and 5.2 per cent in other groups.

Participation of hospitals as educational institutions also showed an increased importance. Hospitals approved for training of medical interns, medical technologists, X-ray technicians, physical therapists, occupational therapists, and medical record librarians are listed.

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## PENICILLIN DENTRIFICE PROMISES CARIES REDUCTION

A new dentifrice containing penicillin gives promise of substantially reducing tooth decay, it has been reported by Dr. H. A. Zander, of Tufts College Dental School, Boston, in The Journal of the American Dental Association, May, 1950.

Dr. Zander said that a two-year experiment had revealed that a group of school children who used a tooth powder containing penicillin were found to have an average of 54% less tooth decay than a similar group of children who used a neutral dentifrice.

The A.D.A. Journal editorially described the report as holding "promise of providing the profession with a new weapon in its fight to control dental caries." It cautioned, however, against viewing the new product, which is not yet on the market, as "a miracle agent."

Dr. Zander based his report on a two-year research study of 352 children between 6 and 14 years of age in two elementary schools in Walpole, Mass.

During the test period, an experimental group of 235 boys and girls in one school brushed their teeth with a tooth powder containing 500 units of potassium penicillin per Gm. of tooth powder. The other 117 pupils in the second school served as a control group and used the same tooth powder without the penicillin.

At the end of the first year, x-ray examinations revealed that the children who used the penicillin dentifrice had developed an average of only 1.34 new cavities compared with an average of 3.00 for the control group, a reduction of 55.3%. At the end of the second year, x-ray examinations disclosed that the penicillin group had 53.8% less new cavities than the control group.

Dr. Zander reported that he had found very few irritating reactions among the school children who used the penicillin dentifrice.

# THE STABILITY OF GIFFORD'S BUFFER SOLUTIONS

by HENRY E. WEST* and STEPHEN WILSON†

THE USE of Gifford's buffer solutions in ophthalmic prescriptions has raised a number of questions regarding the stability of the *p*H value of the solutions used. Do such solutions change in *p*H value? If so, to what extent? How rapid is the change? In what quantities may such solutions be made, as stock solutions? Under what conditions of storage should they be kept? This study is an attempt to answer some of these questions.

Buffered solutions of *p*H 5.0, 6.0, 7.0, 8.0 and 9.0 were prepared and stored under varying conditions. Samples of the solutions of each *p*H value were stored in amber, green and untinted (flint) glass bottles, of soft untreated glass, of glass treated to produce surface hardness, and of hard glass; on an open shelf in the laboratory (to simulate store conditions); on a shelf in the cellar, and in the refrigerator at 10° C. Eight fluidounce bottles were used in all cases. The *p*H of the freshly prepared samples was determined, and then checked once a month for one year. Thus thirteen readings were recorded for each sample, or a combined total of 1755 *p*H determinations.

On the advice of local ophthalmologists, no preservatives were used in the solutions. Consequently a number of the samples developed mold growths. No consistent effect of such molds on the *p*H readings was noted.

The *p*H value of the respective samples tended to rise. The greatest rise in *p*H noted was a unit rise from *p*H 5.0 to *p*H 6.0, which is a tenfold increase in hydroxyl-ion concentration. In general, the change in *p*H varied inversely to the length of time up to six months. That is to say, the rate of change was most rapid at first, and gradually decreased as time went on. Very little change took place after six months—so little, in fact, that the last six months' readings were omitted from the statistical treatment of the observations in compiling the tables shown below.

Table I shows the maximum increase, and also the arithmetic mean of all readings in each *p*H value over a six-month period. The maximum increases occurred at least once in the *p*H group indicated, and range from 0.7 to 1.0. That is to say, at least one sample of the *p*H 5.0 group increased to *p*H 6.0 during the six months. Of the 6.0 group, however, the highest reading was *p*H 6.7.

TABLE I.—MEAN AND MAXIMUM INCREASES IN *p*H VALUES IN GIFFORD'S BUFFER SOLUTIONS OVER A SIX-MONTH PERIOD

| | Original *p*H | | | | |
|---|---|---|---|---|---|
| | 5.0 | 6.0 | 7.0 | 8.0 | 9.0 |
| Arithmetic mean | 0.43 | 0.27 | 0.40 | 0.32 | 0.25 |
| Maximum increase | 1.0 | 0.7 | 0.9 | 1.0 | 0.9 |

A comparison of the arithmetic mean of the increases in *p*H value in all samples in each of the *p*H groups shows a general tendency for the increase to be greater in the lower *p*H groups. Thus a mean increase of 0.43 in the *p*H 5.0 group is compared with the corresponding increase of

Presented before the Section on Practical Pharmacy, A. Ph. A. Convention, Jacksonville, Florida, April, 1949.

* Instructor in pharmacy, University of Pittsburgh School of Pharmacy.

† Professor of pharmacy, University of Pittsburgh School of Pharmacy.

TABLE II.—MEAN AND PERCENTAGE MONTHLY AND CUMULATIVE INCREASES IN *p*H VALUES OF GIFFORD'S BUFFER SOLUTIONS OVER A SIX-MONTH PERIOD

| | Month | | | | | |
|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 |
| Mean monthly increase | 0.18 | 0.09 | 0.07 | 0.06 | 0.01 | 0.01 |
| Percentage monthly increase | 42.9 | 21.4 | 16.6 | 14.3 | 2.4 | 2.4 |
| Mean cumulative increase | 0.18 | 0.27 | 0.34 | 0.40 | 0.41 | 0.42 |
| Percentage cumulative increase | 42.9 | 64.3 | 80.9 | 95.2 | 97.6 | 100.0 |

0.25 in the *p*H 9.0 group. This decrease is gradual and consistent except for the mean increase in the *p*H 6.0 group which is out of line with the others, being 0.27, which is lower than would seem indicated by the other mean increases. A possible explanation for this is mentioned below.

Table II shows the mean increase in *p*H values by months and indicates that the rate of increase in *p*H value is most rapid at first and decelerates as time goes on. In fact, 42.9% of the increase occurred during the first month, nearly 65% by the end of the second month, but only 4.8% during the last two months.

Table III shows the mean and maximum increases of samples stored in amber, green and colorless (flint) glass bottles.

TABLE III.—MEAN AND MAXIMUM INCREASES IN *p*H VALUES OF GIFFORD'S BUFFER SOLUTIONS IN AMBER, GREEN AND FLINT GLASS BOTTLES OVER A SIX-MONTH PERIOD

| | Color | | |
|---|---|---|---|
| | Amber | Green | Colorless (Flint) |
| Mean increase | 0.34 | 0.34 | 0.27 |
| Maximum increase | 1.0 | 1.0 | 1.0 |

Table III shows that storing Gifford's buffer solutions in bottles of colored glass is of no help in preventing the increase in *p*H value of the solutions. An increase of 1.0 *p*H value occurred in each of the three colors used. Colorless (flint) glass showed a slight advantage in the mean increase figure, but not enough to be significant. This advantage is not born out in the maximum figures, which would further indicate the advantage to be unreliable.

Table IV shows a comparison of the mean and maximum increases in *p*H values of solutions stored in bottles made of different types of glass.

TABLE IV.—MEAN AND MAXIMUM INCREASES IN *p*H VALUES OF GIFFORD'S BUFFER SOLUTIONS STORED IN BOTTLES MADE OF DIFFERENT TYPES OF GLASS OVER A SIX-MONTH PERIOD

| | Type of Glass | | |
|---|---|---|---|
| | Untreated Soft Glass | Glass Treated for Surface Hardness | Hard Glass |
| Mean increase | 0.35 | 0.30 | 0.15 |
| Maximum increase | 1.0 | 0.9 | 0.4 |

Table IV shows that hard glass bottles are by far the best type of container for storing Gifford's buffer solutions. The mean increase was significantly lower than for the other types of glass bottles. Also the maximum increase of the individual samples was less than half that of the other types.

Bottles made of glass treated to produce surface hardness average a little better than soft glass bottles, but the maximum increase, being practically as high as that for soft glass indicates that this advantage is not reliable. This may be due to the uneven results of the treating process for hardening the surface of the glass. This would possibly also account for the slight improvement shown by flint glass in the mean figures in Table II, while the maximum figures in the same table do not show a corresponding advantage over the colored glass.

Table V shows mean and maximum increases in *p*H values in Gifford's buffer solutions stored under different conditions.

TABLE V.—MEAN AND MAXIMUM INCREASES IN *p*H VALUES OF GIFFORD'S BUFFER SOLUTIONS KEPT UNDER DIFFERENT CONDITIONS OF STORAGE OVER A SIX-MONTH PERIOD

| | Condition of Storage | | |
|---|---|---|---|
| | Open Shelf | Cellar | 10° C. |
| Mean increase | 0.36 | 0.26 | 0.17 |
| Maximum increase | 1.0 | 0.8 | 0.5 |

(*Continued on Page 446*)

Legal Actions of the

# U. S. FOOD AND DRUG ADMINISTRATION

***. . . a monthly summary of the terminated cases of the U. S. Food and Drug Administration in fields of interest to the pharmacist . . .***

## COURT JUDGMENTS—MAY, 1950

### ADULTERATED AND MISBRANDED DRUGS AND DEVICES

| Locality | Product | Violation | Date Closed and Sentence |
|---|---|---|---|
| 1. Toledo, Ohio | Sulfa-Ton;Sulfa-Col;Dia-Ton; Ty-Ton; Ton-It; Kosa-Ton | Therapeutic claims, quantity, proportion of digitalis glucosides not shown | 5-1-50 Plea: Guilty. Fined $200 on all 6 counts, plus costs of $15 |
| 2. Philadelphia, Pa. | Metandren; Neo-Hombreol | False and misleading claims and labeling, no adequate directions, dangerous if taken as directed | 5-3-50 Plea: Nolo contendere. Fine of $25 on each of 3 counts, against corp., $75; fined $1 on each of 3 counts against individual, $3; total $78 |
| 3. St. Louis, Mo. | Sun-O-Ray Compound and Inhalator | No adequate directions | 5-10-50 Plea: Nolo contendere. Fine of $10 and costs of $35 and 1 hour in the custody of the U. S. marshal |
| 4. Nashville, Tenn. | Castor Oil; Turpentine | False and misleading labeling of turpentine as castor oil | 5-15-50 Plea: Nolo contendere. Fine of $100 on count 1 and $1 on count 2 of 2 informations against the firm and surviving defendant; total $202 |
| 5. Indianapolis, Ind. | Folamin | Non-sterile | 5-19-50 Plea: Guilty. Fined $25 on each of 14 counts, total $350 |
| 6. Columbus, Ohio | Bible Way Tonic and "Annointing Oil" | False and misleading therapeutic claims | 5-22-50 Plea: Guilty. Fined $50 on each of 4 counts, total $200; and sentenced to 1 year in jail on each of 4 counts. Jail sentence suspended, individual placed on probation for 4 years on condition that he no longer engage in the drug business in any manner |
| 7. Chicago, Ill. | Zerret Applicator | False and misleading therapeutic claims | Plea: Not guilty, both defendants. Verdict: Guilty, both defendants. Sentence: 5-22-50; first defendant sentenced to 2 years in penitentiary; second defendant sentenced to 1 year in penitentiary |
| 8. Nashville, Tenn. | Menestrex | Failure to declare directions for use, false and misleading claims | 5-31-50 Plea: Guilty to counts 1, 2, 4 and 5 (failure to declare directions for use). Pleaded and found not guilty to count 3 (false and misleading claims). Fined $1 each on counts 1, 2, 4 and 5, total $4 |

OVER-THE-COUNTER SALES—DRUGS

| Locality | Product | Violation | Date Closed and Sentence |
|---|---|---|---|
| 1. Tuscaloosa, Ala. | Dexedrine; Sulfathiazole | Over-the-counter sale, name of manufacturer, name of drug, ingredients, adequate directions warning against unsafe dosage not given | 5-8-50 Plea: Guilty. Fined $100 for each defendent, total $200 |
| 2. Chicago, Ill. | Amytal Tablets | Over-the-counter sale, name of manufacturer, habit-forming warning, adequate directions for use not given | 5-10-50 Plea: Nolo contendere. Fine of $100 on all 3 counts plus costs of $39.24 against partnership; fine of $50 on all 3 counts against the individual; total fine and costs $189.24 |
| 3. Frederick, Okla. | Sodium Pentobarbital; Sodium Seconal | Over-the-counter sale, name of manufacturer, habit-forming warning, adequate directions for use not given | 5-12-50 Plea: Nolo contendere. Fine against first defendant $50 on each of 5 counts, $250. Fine against second defendant, $50 on each of 2 counts, $100; total $350 |
| 4. Chicago, Ill. | Seconal Sodium Capsules | Over-the-counter sale of dangerous drugs, name of manufacturer, habit-forming warning, adequate directions not given | 5-18-50 Plea: Nolo contendere. Fine of $250 against the corp. and $250 against the individual, plus costs of $36.96; total $536.96 |
| 5. Los Angeles, Calif. | Metandren Linguets; Oreton-M | Over-the-counter sale, deficient in methyl testosterone, no adequate directions or warning against unsafe dosage, dangerous to health when used as indicated | 5-22-50 Plea: Nolo contendere to counts 1 and 2, not guilty to counts 3, 4 and 5. Counts 3, 4 and 5 dismissed. Fined $25 on counts 1 and 2, total $50 |
| 6. Grandfield, Okla. | Seconal Sodium Capsules; Seconal Sodium and Pentobarbital Sodium Capsules; Sulfadiazine Tablets; Nembutal Capsules | Over-the-counter sale of dangerous drugs | 5-22-50 Plea: Nolo contendere. Defendant pronounced guilty and fined $50 on each of 6 counts; total $300 |
| 7. Berwyn and Oak Park, Ill. | Seconal Sodium Pulvules | Over-the-counter sale, habit-forming warning, adequate directions for use not given, no statement of quantity of contents | 5-23-50 Plea: Guilty. Fined $100 on each of 3 counts; total $300, plus cost |
| 8. E. St. Louis, Ill. | Benadryl; Dexedrine; Nembutal; Seconal; Sulfonamide | Over-the-counter sale, no adequate directions nor warning against unsafe dosage | 5-23-50 Plea: Guilty. Individual and corp. fined $100 on counts 1 to 8 incl., and $200 on count 9; total $2000 |

## IMPORTANT FDA INFORMATION FOR PHARMACISTS

We are glad to publish the record of U. S. Food and Drug Administration actions, listed above, as a public health service and as a service to pharmacists.

The violations are identified only by reference to the city and state in which they occurred and, necessarily, by the name of the product involved.

In the **adulterated drug cases, the manufacturer is the violator** and the product is, of course, at fault.

In the **over-the-counter sale cases, the retailer,** not the manufacturer of the product, **is the violator.** Over-the-counter sale violations do not reflect on the product sold, unless the drug is also adulterated.

**SEE *Straight from Headquarters* COMMENT ON THIS FEATURE IN AUGUST ISSUE.**

# A. C. S. SYMPOSIUM ON MEDICINAL CHEMISTRY

APPROXIMATELY 250 members of the American Chemical Society, representing many universities and most of the nation's pharmaceutical manufacturing houses, attended the second national medicinal chemistry symposium held at the University of Notre Dame, June 15–17. The organization for the meeting was well handled by Dr. Kenneth M. Campbell and associates of the Notre Dame Chemistry staff. The papers were grouped under broad headings reflecting the pharmacological or medicinal properties of the chemicals under consideration and each paper was followed by considerable discussion led by someone well qualified in the field.

Among the more interesting papers one titled "Analogues of Chloromycetin" was presented by Dr. H. M. Crooks, Jr., Parke, Davis & Co., who reviewed the work that has been carried out by the same workers who investigated the structures of Chloromycetin toward the development of new compounds with structures simpler but similar to that of Chloromycetin. The work reported indicated that although numerous compounds with activity had been synthesized, no compound was as useful as Chloromycetin on as wide a variety of organisms. Dr. Crooks indicated, however, that work is being continued in this direction and that it is hoped that other useful synthetic antibiotics will be developed.

The chemistry of cortisone was reviewed by Dr. H. C. Mason, Mayo Foundation, and his paper was followed by one on the chemistry of ACTH by Dr. C. H. Li, University of California (presented in the absence of Dr. Li). In the discussion which followed it was brought out by Armour & Co. scientists that recent research has resulted in ACTH preparations with about 1000 times as great an activity as peptides that were formerly believed to represent the active fraction of the adrenocorticotropic hormone and that future work may develop compounds with even higher activity.

### Radioactive Isotopes

A very valuable review of the use of radioactive isotopes in pharmaceutical studies was presented by Dr. D. L. Tabern, Abbott Laboratories. Dr. Tabern described the function of the radioisotopes section at Abbott Laboratories which makes available various radioactive isotopes in pharmaceutically acceptable form. For example, these workers obtain phosphorus-(32) in the form of sodium phosphate from Oak Ridge, remove any impurities that might be objectionable and prepare isotonic solutions in pyrogen-free water. These solutions are then shipped directly to hospitals in suitable flasks so that the physicians and technicians can inject the material in the ascertained manner without going through tedious purification, etc. The same sort of work is being done with iodine-(131); gold-(198)-labeled serum albumen; iodine-(131)-labeled iodofluorescein; and a number of sulfur-(35)-labeled compounds. Dr. Tabern reviewed the difficulties and precautions necessary in carrying out the pharmaceutical as well as clinical work involved in radioisotope studies.

The medicinal chemistry session was particularly fortunate in having Dr. A. Stoll, of Sandoz, Inc., Switzerland, present a paper on the chemistry of the cardiac glycosides which dealt primarily with the determination of structure of some synthesis of the glycosides of squill.

Dr. K. K. Chen, Eli Lilly and Co., presented an excellent review paper on the activities of various cardiac glycosides and in his paper presented data which correlated structure and activity of various groups of these drugs. Dr. Chen stated that the number of hexose molecules attached to the aglycone (steroid nucleus) had a pronounced effect on the cardiac activity and that this effect was predictable in a given series of drugs containing the same basic type of aglycone nucleus, although it differed from one series to another.

### Cardiac Drugs

Dr. Rene W. E. Wegria, Presbyterian Hospital, New York City, reviewed the pharmacological and chemical aspects of cardiac drugs stressing that he had been unable to obtain suitable response in patients to aminophylline by administration of the drug orally, parenterally, or by administration of rectal suppositories. He reported, however, that very good response was obtained when the dose of aminophylline was dissolved in 75 cc. of water and administered rectally. In his paper he included some remarks on khellin which brought forth considerable discussion on the value of khellin in the treatment of angina. Research workers of Smith, Kline and French Laboratories, who have done considerable work with khellin, expressed the opinion that khellin activity was of about the same nature as that of nitrites, though more prolonged. This prolonged activity is making the drug useful in prophylaxis as well as treatment of angina attacks.

On the first evening of the symposium, Dr. E. H. Volwiler, Abbott Laboratories, addressed the group on "The Lucky Chemist," in which he described numerous occasions where chance was a major factor in an important discovery. However, the need for alertness, knowledge and ability in order to convert an accidental discovery into a worth-while contribution was stressed by Dr. Volwiler.

Another highlight of the symposium occurred the second evening when a panel discussion on the mechanism of drugs was held.

The opportunity was given all members attending the medicinal symposium to visit the LOBUND, the bacteriological laboratories of Notre Dame, which are developing strains of germ-free animals. Most of the members took advantage of this opportunity and were richly rewarded by the interesting tour during which they were able to observe the highly specialized technique, and the many problems involved in the raising of animals completely free of bacteria.

# ADR

DENTAL REMEDIES RECENTLY ACCEPTED BY A. D. A. COUNCIL ON DENTAL THERAPEUTICS

*The classification of products by the Council on Dental Therapeutics of the American Dental Association has been described in a previous report* [THIS JOURNAL, **11**, *371 (1950)*]. *The Council's program now provides for classification of products in Group A, Group B, Group C and Group D. Products are reconsidered periodically and decisions are subject to change at any time that a substantial amount of new evidence becomes available.*

## *GROUP A*

Listing of products in group A means that at the time of their consideration, the items conformed with the provisions of acceptance established by the Council on Dental Therapeutics and adopted by the Board of Trustees of the American Dental Association. Items in this group will be listed in *Accepted Dental Remedies*, and may use the Seal of Acceptance, unless otherwise provided.

The following additional products are classified in group A:

*Monocaine HCl 2%, Epinephrine 1:50,000* (Novocol Chemical Mfg. Co.): Each cc. is stated to contain butethamine HCl, 0.02 Gm.; epinephrine, 0.00002 Gm.; sodium chloride, 0.004 Gm.; sodium bisulfite, 0.0015 Gm., and distilled water. See *A. D. R.*, ed. 15, p. 23.

*Novocell Pellets with Phenyl Mercuric Nitrate* (Novocol Chemical Mfg. Co.): Designed for hemostasis. Each pellet of oxidized cellulose is stated to contain phenyl mercuric nitrate, 0.08 mg. See *A. D. R.*, ed. 15, p. 94.

## *GROUP B*

Listing of products in group B means that there is insufficient evidence to justify their present acceptance, but there is reasonable evidence of their usefulness and safety. These products meet the other qualifications and standards established by the Council on Dental Therapeutics and the Bureau of Chemistry. It is the Council's opinion that group B products may be promoted for special use and study.

No products are listed in group B at the present time.

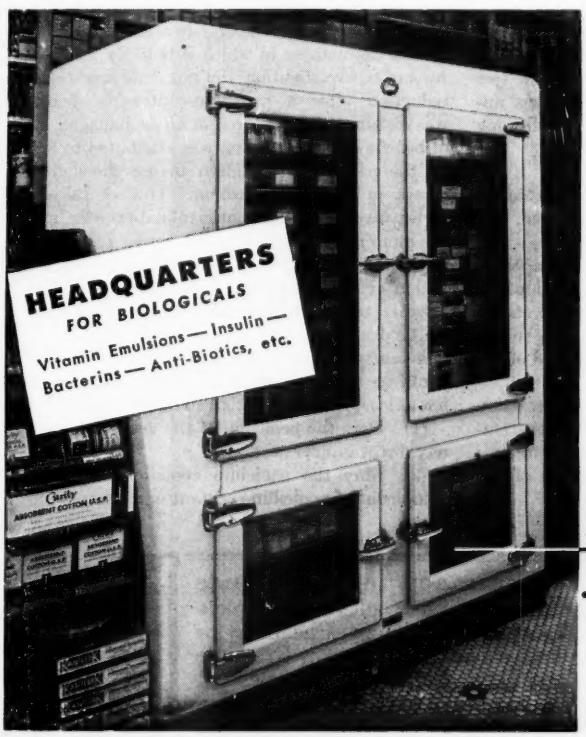
## *GROUP C*

Listing of products in group C means that the evidence is so limited or inconclusive that the products cannot be accurately evaluated. It is the Council's opinion that group C products require further study by qualified investigators.

The following general classes of products are classified in group C:

Dentifrices containing urea or urea and ammonium compounds as the active ingredients.

(*Continued on Page 438*)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Dentifrices containing fluoride as the active ingredient.

Dentifrices containing chlorophyll derivatives as the active ingredient.

### *GROUP D*

**Listing of products in group D means that they are unacceptable because of their demonstrated inability to meet the standards outlined in the provisions for acceptance.**

**The following additional product is classified in group D:**

*Monocaine Anestubes with Penicillin* (Novocol Chemical Mfg. Co.): [For detailed report, see *J. Am. Dental Assoc.*, **40**, 622 (1950)].

### *A PRELIMINARY REPORT ON PENICILLIN DENTIFRICE*

Information concerning tests made with a penicillin-containing dentifrice has been furnished to the Council on Dental Therapeutics by The Andrew Jergens Company. According to this information the firm has applied to the Food and Drug Administration for certification of the penicillin product in accordance with the regulation promulgated under the Federal Food, Drug and Cosmetic Act. No announcement concerning the action of the Food and Drug Administration is available at the present time, but the Council has authorized the publication of the following preliminary report in order that the dental profession may have early information concerning this product.

The principal supporting evidence bearing upon the effectiveness of a penicillin dentifrice was derived from a two-year clinical study[1,2] carried on in two elementary schools. Adequate provision was apparently established with respect to the following factors:

(1) Duration of observation.

(2) Suitable matching of control and penicillin groups with regard to: (*a*) age of the children, and (*b*) number of non-carious teeth.

(3) Number of subjects. There were reported to be 216 children in the penicillin study group and 162 in the non-penicillin study group at the end of the first year, and 202 and 150 respectively in the penicillin and non-penicillin groups at the end of the second year.

(4) Method of examination. The information indicates that roentgenographic studies were employed and that an attempt was made to reduce examiner bias by withholding the identity of the experimental and control group.

The report states that each child involved in the observations in one school was supplied with a tooth powder containing 500 units of penicillin in each gram of powder and that each child in the other group in the second school received an identical dentifrice except for the omission of the penicillin. During the school terms, the experiment involved a daily supervised tooth brushing assignment in the schools in addition to an undetermined amount of tooth brushing at home. Considerable effort was apparently devoted to the problem of teaching the children to brush their teeth and to the problem of enlisting the cooperation of both the children and their parents in order that there would be more consistent use of the dentifrice in the homes.

That portion of the reported data which pertains to permanent teeth indicates that when the penicillin group was compared to the control group there was an average reduction in the number of new decayed or filled surfaces of approximately 54% during each of the two years. It is noted also that the average new caries attack rates reported for the control group, 2.28, and 2.49 surfaces per child respectively for the first and second years, are not higher than might be anticipated for any comparable group of children under similar circumstances. It is the Council's opinion that these data provide good evidence that the penicillin dentifrice is effective in producing a significant reduction in dental caries when the preparation is used under conditions strictly comparable to those in this study.

A practical evaluation of a penicillin dentifrice for general use, however, should include a consideration of the manner in which it is likely to be used. An earlier investigation[3] did not demonstrate caries reduction after a penicillin-containing dentifrice was distributed to children in an orphanage. Lack of benefit in that situation was attributed to failure on the part of the children to use the dentifrice except in a sporadic fashion. The results of the earlier investigation do not invalidate the findings in the more recent study. Those earlier results, however, do suggest that adequate instruction and motivation or supervision of the brushing procedure is essential to the realization of the benefits of a therapeutic dentifrice.

A crucial factor in the evaluation of a penicillin dentifrice is the question of safety. This problem has at least four aspects that should be considered:

(1) Does the penicillin of the dentifrice produce any direct injury?

(2) May the penicillin contribute to the development of penicillin-resistant organisms?

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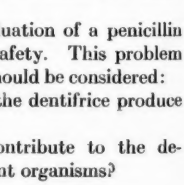

(3) May the use of the penicillin dentifrice sensitize the user to a degree that might result in (*a*) a serious reaction upon subsequent administration of a therapeutic dose of the antibiotic or (*b*) failure to tolerate penicillin in a case of critical need?

Impressive evidence has been presented to indicate that the first question need not cause undue concern. The information indicates that in addition to the more than 200 school children previously mentioned, 4480 other individuals have used a penicillin dentifrice for a period of three months. It appears that reactions to the dentifrice were infrequent and not severe. A limited number of individuals with known sensitivity to penicillin have used the dentifrice. No serious reactions were reported.

A considerable amount of data is also available to answer the second question. Extensive tests have been reported[4] to indicate that use of a penicillin dentifrice does not lead to the development of penicillin-fast salivary lactobacilli or to recognizable increase in the penicillin resistance of streptococci and staphylococci isolated from the throats of the school children. The *in vitro* development of penicillin-resistant organisms is a well recognized phenomenon but there is little evidence to indicate that this change occurs under other conditions.

Less satisfactory answers are available for the third question. Intramuscular injection of 10,000 units of penicillin is reported in 41 individuals who had used the penicillin dentifrice in an earlier three-month period. No reactions were reported but the cases were too few to justify extensive conclusions.

The picture is further confused by the uncertainties which attend an attempt to correlate the results of patch tests and intradermal tests with systemic reactions.[5]

It is not possible, therefore, on the basis of present information to provide a definite statement concerning the safety or lack of safety of this product if it becomes available for indiscriminate use. Nevertheless the predominant position of penicillin as an anti-infective agent in modern therapeutic practice suggests that every reasonable precaution be observed in an attempt to avoid conditions which might deny the benefit of penicillin to the critically ill.

In view of these considerations it seems desirable for the present to limit the use of a penicillin dentifrice to cases of rampant caries in which all potentially effective methods of control should be utilized in the interest of the patient. This program would have the following advantages:

(1) Use of the agent under professional supervision will facilitate the recognition of possible side effects. It will also provide greater assurance that the material will be properly used in order that maximum benefit is obtained by the patient.

(2) Opportunity would be provided for the orderly collection of further clinical data which could be used as the basis of a later decision concerning the method of distribution of this type of product.

(3) Some additional opportunity would be provided for the clarification of the status of newer antibiotics and other drugs which may be substituted for penicillin.

On the basis of available evidence, the Council on Dental Therapeutics is of the opinion that penicillin dentifrices should not be distributed at the present time except on a prescription basis.

### REFERENCES


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2. Zander, H. A.; Lind, H. E., and Drolette, Margaret, Effect of a Penicillin Dentifrice on a Group of School Children. Presented at the Twenty-eighth General Meeting of the International Association for Dental Research, March 24–26, 1950.
3. Hill, Thomas J., and Kniesner, Albert H., Penicillin-Dentifrice and Dental Caries in Children. *J. D. Res.*, **27**, 744 (1948).
4. Fitzgerald, Robert J., and Zander, H. A., Incidence of Penicillin Fast Lactobacilli in Salivas of Children Using a Penicillin Tooth Powder, Presented at the Twenty-eighth General Meeting of the International Association for Dental Research, March 24–26, 1950.
5. Peck, Samuel M.; Siegal, S.; Glick, A. W., and Kurtin A., Clinical Problems in Penicillin Sensitivity. *J. Am. Med. Assoc.*, **138**, 631 (1948).


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# Obituaries

## Lehman Alley

Lehman Alley, secretary of the Alabama Board of Pharmacy, died suddenly May 30, at the age of 48. Mr. Alley had just completed a tour of inspection of the Alabama Polytechnic Institute School of Pharmacy with Dr. E. C. Elliott and Dr. George D. Beal.

## Alexander J. Horlick

Alexander J. Horlick, last of the immediate family of the founder of the Horlick Malted Milk Corporation, died June 6, at Racine, Wisconsin.

Mr. Horlick, a life member of the AMERICAN PHARMACEUTICAL ASSOCIATION, was 76 years old. He had been associated with the Horlick firm for 52 years in 1945 when he relinquished his post as chairman of the board.

## Frank F. Law

Frank F. Law, vice-president of Wyeth Incorporated, died June 5 after several months' illness. Mr. Law, who had given nearly 40 years of service to his profession of pharmacy, was 56 years old.

## Herman H. North

Herman H. North, president of the New Jersey Pharmaceutical Association, died May 18 of a heart attack at the age of 57. Dr. North had been a practicing pharmacist in Bloomfield, New Jersey, for more than 30 years.

## William Freeman Snow

William Freeman Snow, M.D., founder and chairman of the Board of Directors of the American Social Hygiene Association, died June 12 at the age of 76. Dr. Snow's life work has brought together those medical, educational and moral forces which today form the framework of the national social hygiene movement.

# NNR

PRODUCTS RECENTLY ACCEPTED BY THE A. M. A. COUNCIL ON PHARMACY AND CHEMISTRY

*Council descriptions of new drug products only are published regularly in* THIS JOURNAL *as they are accepted. Rules upon which the Council bases its action appeared in the July (7:320) 1946 issue, and may be secured in pamphlet form upon request to the Secretary, Council on Pharmacy and Chemistry, American Medical Association, 535 N. Dearborn St., Chicago 10, Ill.*

**DIPHTHERIA TOXOID, ALUMINUM HYDROXIDE ADSORBED**—Aluminum Hydroxide Adsorbed Diphtheria Toxoid is a sterile suspension of diphtheria toxoid adsorbed on aluminum hydroxide from the solution in which the products of growth of the diphtheria bacillus (*Corynebacterium diphtheriae*) have developed and have been so modified by special treatment as to have lost the ability to cause toxic effects in guinea pigs but retain the property of inducing active immunity. The antigenic value is such that not more than one-half the volume, which is to be recommended for the lot under test as the total human immunizing dose, produces at least 2 units of antitoxin per cc. of serum in not more than four weeks in an aliquot serum-pool from not less than four guinea pigs. Aluminum Hydroxide Adsorbed Diphtheria Toxoid complies with the official potency and other requirements of the National Institutes of Health of the United States Public Health Service.

*Actions and Uses.*—(See N. N. R. monograph on Diphtheria Toxoid.) Because of the physical character of the aluminum hydroxide adsorbed product, absorption is delayed.

*Dosage.*—Hypodermic, for active immunization 0.5 cc. to be repeated twice with an interval of three to four weeks.

*Cutter Laboratories, Berkeley 1, Calif.*

**Diphtheria Toxoid, Alhydrox:** 1-cc. vials (one immunization) and 5-cc. vials (five immunizations). Preserved with thimerosal 1:10,000.

**DIPHTHERIA AND TETANUS TOXOIDS, ALUMINUM HYDROXIDE ADSORBED.**—Diphtheria and Tetanus Toxoids, Aluminum Hydroxide Adsorbed is a turbid, white or slightly gray suspension prepared by mixing suitable quantities of aluminum hydroxide adsorbed diphtheria toxoid and aluminum hydroxide adsorbed tetanus toxoid, each of which possesses adequate potency to permit combining. The toxoids shall be mixed in such proportions as to provide an immunizing dose of each toxoid in the total dosage prescribed on the label. Aluminum Hydroxide Adsorbed Diphtheria and Tetanus Toxoids complies with the requirements of the National Institutes of Health of the United States Public Health Service.

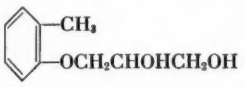
*Actions and Uses.*—(See N. N. R. monograph on Diphtheria and Tetanus Toxoids.) Because of the physical character of the aluminum hydroxide adsorbed product, absorption is delayed.

*Dosage.*—Hypodermic, for active immunization, 0.5 cc. to be repeated once with an interval of four to six weeks.

*Cutter Laboratories, Berkeley 1, Calif.*

**Diphtheria and Tetanus Toxoids Alhydrox:** 1-cc. vials (one immunization) and 5-cc. vials (five immunizations). Preserved with thimerosal 1:10,000.

**MEPHENESIN.—Oranixon** (Organon).—3-*o*-Toloxy-1,2-propanediol.—$C_{10}H_{14}O_3$.—M. W. 182.21.—The structural formula of mephenesin may be represented as follows:




*Actions and Uses.*—Mephenesin, a synthetic cresol glyceryl ether, produces transient relaxation and paralysis of skeletal muscle in small laboratory animals. It depresses reflex excitability of nerve centers and potentiates barbiturate anesthesia. In doses which do not cause paralysis or narcosis, it antagonizes the action of strychnine.

The drug is quickly destroyed in the body and has a low toxicity. Intravenous injection of a 10% concentration will cause hemolysis of red cells with hemoglobinuria.

The drug acts on the reflex centers of the brain and spinal cord and in high doses depresses cortical cell function and transmission of nerve impulses across synapses. Although the effects of mephenesin resemble those of curare, the mechanism of action is different. High concentrations of mephenesin have local anesthetic properties. Thus, oral administration may cause transient anesthesia of the oral mucosa.

Although the use of the drug is still largely experimental, its low toxicity permits its cautious trial for the production of muscular relaxation in light surgical anesthesia, if it is remembered that it may potentiate the action of barbiturates. It may also be tried in the treatment of spasticity and tremor of Parkinson's disease; in the treatment of muscle spasm in

(*Continued on Page 442*)

# *infants and children in your neighborhood*

The frequent anemias noted among these youngsters will soon be more effectively treated with Zymatinic* Drops – the new hematinic specifically formulated to meet the requirements of clinicians treating the anemias of infancy and childhood.

Zymatinic Drops effectively combines the multiple factors now known to be specifically required in the modern treatment of anemia during the period of active growth. It is a stable, acceptable liquid preparation and may be administered direct or mixed with fruit juices Zymatinic Drops contains in each cc.:

| | |
|---|---|
| *Liver Concentrate* | *from 7.8 Gm. whole liver* |
| *Ferrous Gluconate* | *65 mg.* |
| *Thiamine Hydrochloride (B1)* | *1 mg.* |
| *Riboflavin (B2, G)* | *1 mg.* |
| *Nicotinamide* | *8 mg.* |
| *Folic Acid* | *1 mg.* |
| *Alcohol* | *1.5%* |

Zymatinic Drops is now being introduced to physicians in your neighborhood by extensive sampling, detailing, direct mail and journal advertising programs.

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**Upjohn**
KALAMAZOO 99, MICHIGAN

***Fine Pharmaceuticals Since 1886***

## NEW AND NONOFFICIAL REMEDIES

**Mephenesin** • • • • • • • • • • *from page 440*

certain cases of hemiplegia, tetanus and certain other spastic conditions; and in the treatment of athetoid or choreiform movements.

The effects of mephenesin are quite temporary and since little is known of its chronic toxicity, prolonged use requires constant watch for possible untoward effects. It should be used as an adjunct to surgical anesthesia only by those with special experience in the field.

*Dosage.*—For adults, 1 Gm. given orally three to five times a day. The dosage should be spread evenly throughout the waking hours. If a favorable response is not seen within 72 hours, the drug should be discontinued.

*Tests and Standards.*—

*Physical Properties:* Mephenesin is an odorless, crystalline, white powder which melts between 67 and 72° C. It is freely soluble in alcohol, chloroform and ether; and sparingly soluble in benzene and water. The *p*H of a saturated solution is about 6.0.

[For tests and standards see *J. Am. Med. Assoc.*, **143**, 655 (1950).]

*Organon, Inc., Orange, N. J.*

**Elixir Oranixon:** 237-cc., 473-cc. and 3.78-liter bottles: A 20% alcohol solution containing 0.1 Gm. of mephenesin in each cc. Preserved with 0.037% of methylparaben-U.S.P. and 0.025% of propylparaben-U. S. P.

**Tablets Oranixon:** 250 mg.

**TETANUS TOXOID, ALUMINUM HYDROXIDE ADSORBED.**—Aluminum Hydroxide Adsorbed Tetanus Toxoid is a sterile suspension of tetanus toxoid, adsorbed on aluminum hydroxide from a solution in which the products of growth of the tetanus bacillus (*Clostridium tetani*) have developed and have been so modified by special treatment as to have lost the ability to cause toxic effects in guinea pigs, but retain the property of inducing active immunity. The antigenic value is such that not more than one-half of the volume, which is to be recommended for the lot under test as the total human immunizing dose, produces at least 2 units of antitoxin per cc. of serum in not more than six weeks in an aliquot serum-pool from not less than four guinea pigs.

Aluminum Hydroxide Adsorbed Tetanus Toxoid complies with the official potency test and other requirements of the National Institutes of Health of the United States Public Health Service.

*Actions and Uses.*—(See N. N. R. monograph on Tetanus Toxoid.) Because of the physical character of the aluminum hydroxide adsorbed product, absorption is delayed.

*Dosage.*—Hypodermic, for active immunization, 0.5 cc. to be repeated twice with intervals of three to four weeks.

*Cutter Laboratories, Berkeley 1, Calif.*

**Tetanus Toxoid, Alhydrox:** 1-cc. vials (one immunization) and 5-cc. vials (five immunizations). Preserved with thimerosal 1: 10,000.


**Accepted by Leading Pediatricians**

**Accepted by Council on Foods**

*Laxative Modifier of Milk for Constipation in Infants*

Borcherdt MALT SOUP EXTRACT (Liquid)

DRI-MALT SOUP EXTRACT (Powder)

ORDER AN ADEQUATE SUPPLY FROM YOUR WHOLESALER

FEATURES:
- High proportion of readily fermentable maltose encourages the growth of aciduric bacteria and retards growth of putrefactive organisms.
- Malt Soup Extract stimulates peristalsis.
- Water-soluble extractives of choice, malted barley and the added potassium carbonate contribute to the gentle laxative effect.
- Mixture of sugars (maltose-dextrins) means better toleration—no danger of gastrointestinal irritation, excessive fermentation, or diarrhea when used as directed by the physician.

***Palatable . . . Dissolves Readily in Milk***

SUPPLIED: Malt Soup Extract—Jars containing 8 fl. oz. and 1 pt. Dri-Malt Soup Extract—Jars containing 1 lb.

**Borcherdt MALT EXTRACT COMPANY**

*Malt Products for the Medical Profession Since 1868*

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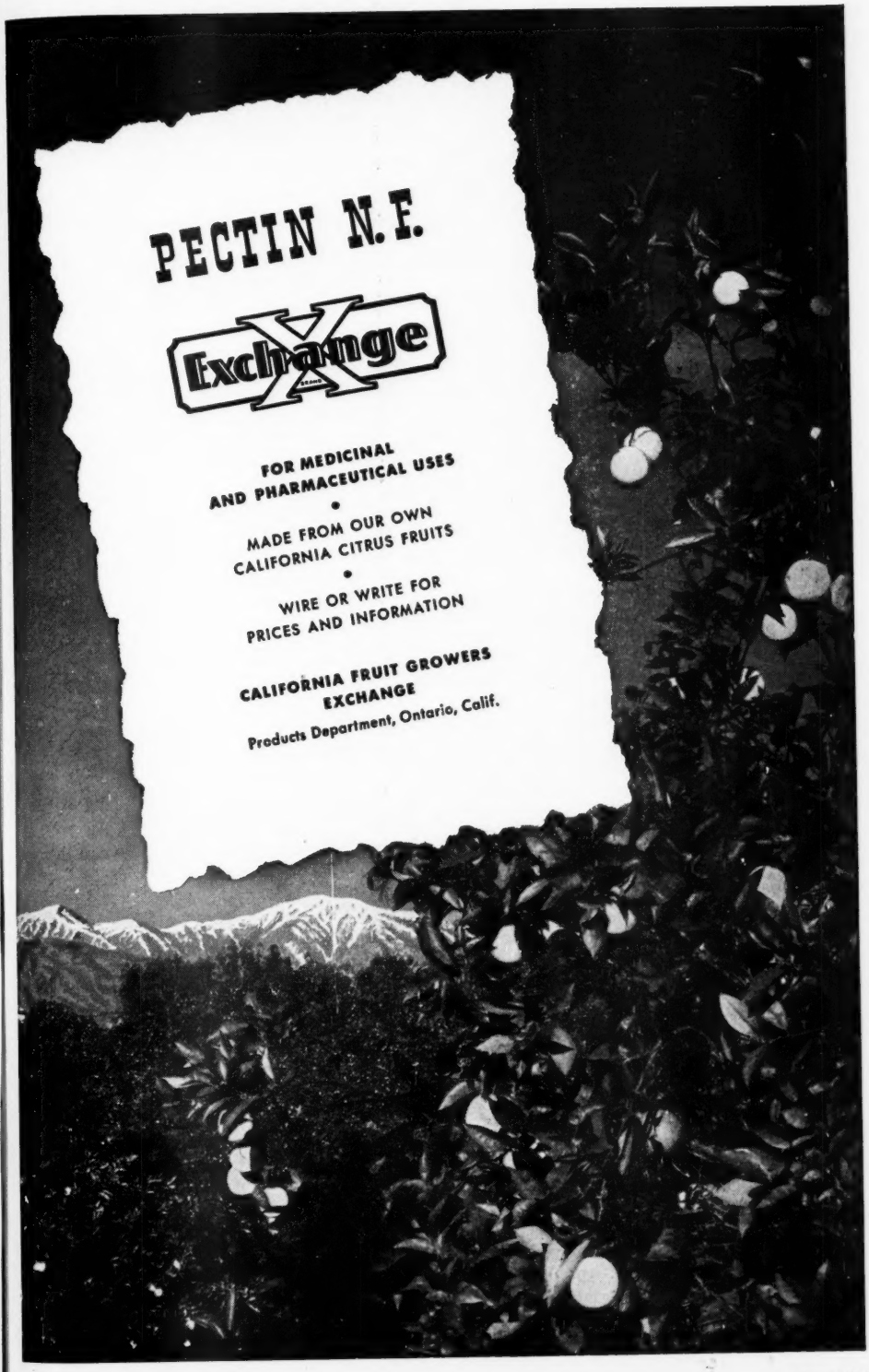
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EXCHANGE
Products Department, Ontario, Calif.

# Typical Days

FROM THE SECRETARY'S DIARY FOR APRIL

**2nd** After a week end completing many convention details, leaving for Atlanta to join the pharmacists of Georgia in celebrating the diamond anniversary of the founding of their state pharmaceutical association. Paul Olsen was on the same train bound for the same place, and the conversation dealt largely with the changing character of state association programs and what pharmacists like to hear about before they begin to resolve "in convention assembled."

**3rd** Shortly after early and prompt arrival in Atlanta and being quartered at the Biltmore, there came President Blasingame of the Ga. Ph. A. with newspapermen and photographers for interview and pictures which made the front page of the afternoon paper. Now to the Southeastern Conference, presided over with dignity and charm by Thelma Morris Coburn. Here the chief topic was legislation and law enforcement with heavy emphasis on FDA invasion of the prescription regulatory field previously left exclusively to the states. A pleasant luncheon conference with Bert Mull and then to the opening session of the Georgia meeting. It was a magnificent tribute to the organizing genius and hard work of Secretary Russell Rainey who worked himself sick to make this the great event that it was. Now substituting for A. Ph. A. President Jenkins originally scheduled to bring greetings to this convention. Late in the afternoon back to Washington, for our own convention still demands undivided attention.

**4th** Now bringing the staff up to date on A. Ph. A. convention details and listening to an excellent talk by Dr. Powers to the staff on how the N. F. is prepared. Much of the balance of this day spent in working over government forms dealing with research and administrative projects.

**5th** The long distance wires busy collecting late program data from Louis Zopf, efficient A. A. C. P. secretary, and others and now giving the printer final instructions with regard to the Atlantic City meeting program.

**6th** Conferring with U. S. P. Chairman E. F. Cook and Dr. Powers on U. S. P. and N. F. problems and then a session with Al Skean, the very efficient and highly cooperative convention bureau director in Atlantic City. Also, completing arrangements for the professional program of the Ohio State Association meeting which we promised the late Victor Keys.

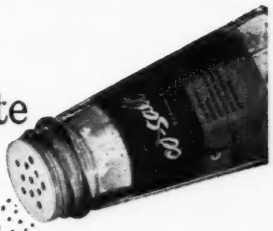
**8th** In the late afternoon, to meet Mr. and Mrs. C. W. Maplethorpe of London, England, who are here on a visit and sigthseeing tour before their anticipated trip to the A. Ph. A. convention where Mr. Maplethorpe will discuss the British Health Insurance Program. Plans for tomorrow include a visit to Mt. Vernon with the Maplethorpes and an inspection of the many places of interest in Alexandria and environs.

**12th** The early days of this week pursuing routine activities and now discussing with top-flight attorneys the language of Food, Drug and Cosmetic Act, under which the FDA claims authority to determine prescription renewal policies. A late arrival in New York last night and ready to meet this morning with Tom Rowe, Harold Darnell, Messrs. Arkus and Cabot on public relations problems, especially the Pharmacy Week program. Now to the University Club to participate in the luncheon given by the trustees of the U. S. P. in honor of the dedication of the new building and later in the afternoon joining some 300 representatives of all branches in the Morgan Library where the dedication ceremonies were held.

**15th** This week ends with a final convention mailing to all active members and the completion of many pre-convention tasks. On Thursday sworn in as Pharmacist-Director (Colonel), U. S. Public Health Service, Reserve (Inactive), which represents a promotion to the highest available grade for pharmacists in this service. Also on that day reviewing the entire convention program with Council Chairman Beal who paid us a brief visit and then to the City of Washington Branch Meeting to speak on A. Ph. A. progress. Yesterday, at lunch with F. Royce Franzoni, Dean Bliven, and Ichiro Keimatsu, Director, Pharmaceutical and Supply Bureau, Ministry of Welfare, Tokyo, Japan, who was on a visit to the United States to learn more about American pharmacy.

**30th** The latter days of this month were filled with last-minute convention tasks and there were many members en route to Atlantic City who stopped to see their building and exchange ideas about services which the Association can and does render. It is always a pleasure to receive members of the Association.

new and different salt substitute



*...tastes like salt*

*looks like salt*

*sprinkles like salt*

co-salt

congestive heart failure

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hypertension

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CO-SALT tastes so much like table salt that low sodium diet patients can actually enjoy their food again. With CO-SALT in place of sodium chloride, they will cooperate more fully in following your diet...will be better nourished...and intake of edema-causing sodium will be held to a minimum.

CO-SALT CONTAINS NO LITHIUM . . . is not bitter, metallic, or disagreeable in taste. It is the only salt substitute that contains choline.

CO-SALT — for use at the table or in cooking—will be a joy to low-sodium diet patients.

INGREDIENTS: Choline, potassium chloride, ammonium chloride and tri-calcium phosphate.

Professional Samples Upon Request

Available:
2 oz. shaker top package
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**Casimir Funk Laboratories, Inc.**
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## *Gifford's Buffer Solution*

. . . . . from page 433

Table V shows a decided advantage in favor of storing Gifford's solutions under refrigeration. The *p*H of the solutions increases less under refrigeration than when stored on an open shelf or in the cellar. The solutions stored in the cellar were somewhat more stable than those on the open shelf, and this may be due to the slightly lower temperature in the cellar. Refrigeration at 10° C. showed by far the best results.

Table VI is an attempt to show the results of storing Gifford's buffer solutions in hard glass bottles and under refrigeration, as compared to other conditions of storage and types of glass.

Table VI shows the decided advantage of storing Gifford's buffer solutions in hard glass bottles and also under refrigeration at 10° C. This combines with good effect the advantage shown separately for hard glass in Table IV and under refrigeration in Table V. Not only is the average increase in *p*H value quite low, but the maximum increase reached by any of the individual samples is only 0.2. This would indicate that this combination of conditions is not only good in general, but is quite reliable.

### Conclusions

From the above data, the following conclusions may be drawn:

1. Gifford's buffer solutions tend to increase in *p*H value during storage.
2. The rate of increase is more rapid at first and gradually slows down.
3. Very little change takes place after six months.
4. The greatest extent of change was a 1.0 increase in *p*H value, or a tenfold increase in hydroxyl-ion concentration, in a six-month period.
5. The increase tends to be slightly greater in the lower *p*H ranges.
6. Colored glass has little if any effect in preventing the change.
7. Hard glass has considerable effect in preventing the change.
8. Refrigeration (10° C.) has considerable effect in preventing the change.
9. For greatest stability, Gifford's buffer solutions should be stored in hard glass containers under refrigeration.

TABLE VI.—MEAN AND MAXIMUM INCREASES IN *p*H VALUES OF GIFFORD'S BUFFER SOLUTIONS KEPT IN VARIOUS COMBINATIONS OF TYPES OF GLASS BOTTLES AND CONDITIONS OF STORAGE OVER A SIX-MONTH PERIOD

| | Type of Glass and Condition of Storage | | |
|---|---|---|---|
| | Hard Glass Under All Conditions | All Types of Glass Under Refrigeration | Hard Glass Under Refrigeration |
| Mean increase | 0.15 | 0.17 | 0.09 |
| Maximum increase | 0.4 | 0.5 | 0.2 |

## UNITED STATES DEATH RATE LOWERED IN 1948

The death rate for the United States in 1948 was the lowest in the history of the country, according to a compilation made by the Public Health Service's National Office of Vital Statistics.

The crude death rate for 1948 was 9.9 per 1000 population—2% below the rate of 10.1 for 1947 and 1% lower than the 1946 rate, the previous low.

The leading causes of death remained the same as in 1947. The major chronic diseases associated with advanced age accounted for 63 of every 100 deaths. Death rates in this group showed only slight changes from the 1947 record. The death rate for diseases of the heart was 322.7 per 100,000 population, while the 1947 rate was 321.2. The death rate for cancer and other malignant tumors increased from 132.4 in 1947 to 134.9 in 1948. The death rate for diabetes remained about the same for the two years; the 1947 rate was 26.2, and the 1948 rate 26.4. Deaths from nephritis, and from intracranial lesions of vascular origin each showed small declines. The 1948 death rate for intracranial lesions was 89.7, while the 1947 rate was 91.4. The nephritis death rate dropped from 56.0 in 1947 to 53.0 in 1948.

Mortality from the major infectious diseases continued their long-time declines. The death rate for pneumonia and influenza, combined, and the rate for tuberculosis both reached new lows.

Motor-vehicle accident deaths decreased for the second successive year.

Mortality from two communicable diseases of childhood—poliomyelitis, acute polioencephalitis and measles—increased sharply from 1947, a low year.

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MERCK

## PRESCRIPTION CHEMICALS

**AT NO EXTRA COST MODERNIZE YOUR PRESCRIPTION DEPARTMENT**

All eight sets of Merck "fused-label" chemical bottles are ready for shipment: featuring *dual labels that are part of the glass itself*—moistureproof, dirtproof, virtually immune to scratch marks. There's no premium charged for the "fused-label." Order any or all of these sets; consult your wholesaler or Merck salesman for complete list.

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## ASSOCIATIONS

"The positive approach to national health sees health as a condition of growth. Our health standards...must grow unceasingly or they will decline," concluded Admiral H. P. Blandy, U. S. N. (ret.), president of the Health Information Foundation, in his address to the **American Pharmaceutical Manufacturers' Association.** Dr. Robert T. Stormont, secretary of the American Medical Association Council on Pharmacy and Chemistry, another speaker at the Association's 43rd convention at Colorado Springs, discussed "Rational Therapeutics."

Howard B. Fonda, senior vice-president of the Burroughs-Wellcome Co. (United States Division), Tuckahoe, N. Y., will take office as president of the A. Ph. M. A. on August 1. Mr. Fonda will succeed Dr. Theodore G. Klumpp, president of Winthrop-Stearns, Inc.

New Jersey pharmacists operate with an average net profit of only 5.7 per cent, according to a survey made by the **New Jersey Pharmaceutical Association.** This is a drop of one full point from the profit percentage shown in the Association's study made in 1931.

James H. Merritt has been named executive secretary of the **Ohio State Pharmaceutical Association.** He succeeds Victor L. Keys, who died in April. Mr. Merritt, whose schooling was interrupted by a tour of duty with the Fifth Air Force in the Pacific Theater, is a graduate of Ohio State University's Business Administration School.

Speakers at the fifth annual meeting of physicians and pharmacists of Albany, N. Y., sponsored by the **Albany Pharmaceutical Association,** included: Dr. Paul L. Wermer, American Medical Association Council of Pharmacy and Chemistry; Dean Francis J. O'Brien, Albany College of Pharmacy; Dr. Thomas J. O'Donnell, president of the Albany County Medical Society; and Jacob Cheris, president of the Association.

Lupton Patten, president of the Chattanooga Medicine Company, Chattanooga, Tenn., was elected president of **The Proprietary Association of America** at the close of the Association's 68th annual convention at White Sulphur Springs, W. Va., May 27. Mr. Patten succeeds Walter Beardsley, president of Miles Laboratories, Inc., Elkhart, Ind., who becomes an honorary vice-president.

Other officers elected were: 1st vice-president, E. T. T. Williams, president of Lambert Pharmacal Co.; 2nd vice-president, S. M. Rising, president of the J. H. Guild Co.; 3rd vice-president, Fred E. Rathburn, president of the Olive Tablet Co. Dr. Frederick J. Cullen was re-elected for a term of four years as executive vice-president and operating head of the Association. A. K. Barta was re-elected for a term of one year as secretary-treasurer.

The following were elected to the Association's Executive Committee for a term of three years: George S. McMillan, vice-president of Bristol Myers Co.; Alvin G. Brush, chairman of the board, American Home Products Corp.; Lunsford Richardson, chairman of the board, Vick Chemical Co.; Wm. F. Laporte, president of Whitehall Pharmacal Co., Division of American Home Products Corp., to fill the unexpired term of Dr. R. P. Herwick (American Home Products Corp.) who resigned.

More State Association Convention News!

Lester Sparks, Huntsville, president of the **Alabama Pharmaceutical Association,** presided over the June 20–22 convention in Birmingham that celebrated the 69th anniversary of the Association. Glenn L. Jenkins, immediate past-president of the AMERICAN PHARMACEUTICAL ASSOCIATION, spoke at the convention.

During its convention, held in May at Daytona Beach, the **Florida State Pharmaceutical Association** heard addresses from: George Bender, editor of *Modern Pharmacy;* J. J. Toohy, vice-president and general manager of E. R. Squibb & Sons; E. L. Newcomb, executive vice-president of the National Wholesale Druggists' Association and 1950 Remington Medalist; and Dr. Robert P. Fischelis, secretary of the A. PH. A.

A gold key in token of 10 years' service as secretary-manager of the Florida Association was presented to R. Q. Richards of Ft. Myers, on behalf of the 7 presidents under whom he had served. Dr. Fischelis made the presentation. Officers elected for 1950–51 are: Edward J. Pierce, Jacksonville, to succeed E. E. Bludworth, Ft. Myers, as president; Euless Watford, Chipley, 1st vice-president; Clyde Norris, Daytona Beach, 2nd vice-president; A. William Morrison, 3rd vice-president; William B. Parr, Tampa, treasurer. The Association also named R. Q. Richards, its secretary-manager, for appointment to the State Board of Pharmacy.

Meeting in May in Chicago, the **Illinois Pharmaceutical Association** heard, in its four-day convention, speakers whose interests covered the world of

pharmacy and the world at large. Speakers included: Congressman Noah M. Mason of Illinois who spoke on "Taxes and the Pharmacist"; John W. McPherrin, editor of the *American Druggist*, who spoke on "Pharmacy vs. Socialized Medicine Program"; and the featured guest speaker of the 70th annual convention, Morgan Beatty, N. B. C. commentator, who discussed current events.

A three-day convention opened June 11 in Swampscott for the **Massachusetts State Pharmaceutical Association.** Speakers from the pharmaceutical world for the 69th annual meeting included: Frank A. Moudry, president of the National Association of Retail Druggists; Martin E. Adamo, president of the New England College of Pharmacy; and John C. F. Cusick, president of the State Board of Registration in Pharmacy. Officers elected for 1950–51 were: Samuel Friedman, Roxbury, president; William Blair, Great Barrington, 1st vice-president; William O'Brien, New Bedford, 2nd vice-president; Wilfred Chagnon, Newton, recording secretary; Martin E. Adamo, Boston, treasurer; and Samuel Silverman, Boston, executive secretary.

Governor Thomas J. Mabry welcomed delegates to the 21st annual convention of the **New Mexico Pharmaceutical Association** meeting in Santa Fe June 6–8. Henry H. Gregg, A. PH. A. president, was one of the principal speakers along with Dr. W. W. Bauer of the American Medical Association and John W. McPherrin, editor of the *American Druggist*. During the sessions, the Association honored Ernest Welch, a practicing pharmacist for 25 years and now a state drug inspector, by presenting him with a plaque in recognition of his 25 years as "good pharmacist and good citizen."

Paul S. Smith, Rochester, president of the **New Hampshire Pharmaceutical Association,** presided over the Association's 76th semiannual meeting at Concord. A report from Secretary George A. Moulton gives September 10, 11, 12 as the dates for the Association's fall convention at Portsmouth.

Virginia pharmacists met in Richmond June 11–14 for the 69th annual convention of the **Virginia Pharmaceutical Association.** Current issues facing retail pharmacists were featured by speakers including: Representative Carl T. Durham, from North Carolina, who spoke on "Pharmacy Today as Seen by a Congressman Pharmacist"; George P. Larrick, associate commissioner of the Food & Drug Administration; John W. Dargavel, executive secretary of the National Association of Retail Druggists; and Robert L. Swain, editor of *Drug Topics* and *Drug Trade News*. Officers elected at the closing session were: Edward E. Willey of Richmond, to succeed Charles Green, of Bedford as president; Cecil Lipes of Roanoke and Byron Fitzhugh of Suffolk, vice-presidents; and J. C. Nottingham of Richmond, secretary-treasurer.

When the **South Carolina Pharmaceutical Association** was organized in 1876, it had 50 members. When the Association held its 74th annual meeting in Columbia June 14–16, seven of its more than 600 members were honored for having served continuously as pharmacists for 50 years or more. The long-time pharmacists were: M. S. Dantzler, Ellaree; Samuel C. Hodges, Greenwood; Joseph B. Hyde, Charleston; Samuel B. Mitchell, Sumter; J. J. Ohear, Winnsboro; E. H. Varn, Columbia; and W. R. Zemp, Camden. Principal guest speaker of the convention was Bert R. Mull, Eli Lilly & Co.

Officers elected for 1950–51 are: M. S. Judy, St. George, to succeed Henry Miller, Charleston, as president; Wm. S. Bates, Greenville, 1st vice-president; I. M. Satterwhite, Newberry, 2nd vice-president; N. E. Hood, Rock Hill, 3rd vice-president. J. M. Plaxco was re-elected secretary-treasurer.

Salt Lake City was the setting for the 58th annual convention of the **Utah Pharmaceutical Association,** June 11–13. Sam Harman, Association president, presided over the meeting. A list of prominent speakers included Henry H. Gregg, A. PH. A. president, and George A. Bender, editor of *Modern Pharmacy*.

At the 44th annual convention of the **California Pharmaceutical Association** in San Francisco, June 5–7, H. F. Webster of Altadena was elected president, succeeding Fred P. Beretta of Berkeley. Convention speakers included: Maurice Mermey, director of the Bureau of Education on Fair Trade; Walter F. Terry, president of Calvert Distillers, Inc.; Dr. Ivan Szekeley, University of California College of Pharmacy; and Dr. Milton M. Hartman, San Francisco physician.

## COLLEGES

Twenty-five members of the **Philadelphia College of Pharmacy and Science** class of 1900 were honored in May at semicentennial exercises at the college. Among those receiving citations was Dr. E. Fullerton Cook, former chairman of the United States Pharmacopeia Revision Committee.

Dr. Ivor Griffith, president of the college, was given a testimonial dinner by the Galen Pharmaceutical Society for his efforts to promote in his own college, equal opportunity and understanding among all racial, religious and nationality backgrounds.

Dr. George Urdang, professor of pharmacy at the **University of Wisconsin** and director of the American Institute of the History of Pharmacy, is spending the summer in Europe. Dr. Urdang will attend pharmaceutical society meetings in Germany and France before going to Switzerland to meet with members of the World Health Organization. In August, Dr. Urdang will go to Amsterdam to attend

the Sixth International Congress for the History of Science, at which he will speak on "How Chemicals Entered the Official Pharmacopeias."

**Temple University School of Pharmacy** will have Dr. Joseph B. Sprowls, Jr., as dean, succeeding the late Dr. H. Evert Kendig. Dr. Sprowls, a native of Colorado, joined Temple's faculty in 1945 after teaching at his alma mater, Colorado University, and at the University of Buffalo.

In an effort to meet a need for trained pharmacists throughout the state, the Illinois Pharmaceutical Association passed a resolution at its recent annual meeting, to ask the **University of Illinois** to increase its number of pharmacy graduates to 200 each year. The 1950 graduates will number 77. Because of limited facilities, the college has been able to accommodate only one out of every five applicants each year since the close of the war. The University of Illinois is the only accredited school of pharmacy in Illinois.

At the request of the Cambria-Somerset Pharmaceutical Association, the **University of Pittsburgh School of Pharmacy** offered a series of lectures and demonstrations in Johnstown, Pa., to a class limited to 40 registered pharmacists. "Allergy and Antihistaminics," "Radioactivity and Isotopes," and "Antibiotics" were among the modern developments in pharmacy that were discussed.

## HOSPITAL PHARMACY

Tentative plans for the 52nd annual convention of the **American Hospital Association** to be held in Atlantic City, September 18–21, announce "Organizing the Hospital to Meet the Changing Scene" as the main theme to be covered. There will be sessions on general questions, finances, medical practice, and a "Small Hospital Forum." This will include a panel of 40 selected administrators to analyze problems of interest to small hospitals.

Group conferences will include sections on hospital purchasing, hospital design, today's problems in anesthesia, special problems in financing hospital care, state hospital survey and construction, problems in hospital finance with reference to accounting, future of nursing education in relation to providing adequate nursing personnel for patient care, and women's hospital auxiliaries.

The Division of Hospital Pharmacy of the A. PH. A. and the A. S. H. P. again will sponsor an exhibit at the A. H. A. convention.

"Regional Planning to Strengthen the Voluntary Hospitals" was the theme for the **Catholic Hospital Association's** 35th annual meeting in Milwaukee, June 12–15. Stress was laid on the necessity of cooperation between small and large hospitals in order to give aid to the smaller units in educational programs for staff members; in administrative areas, and in clinical services. During the meetings the group examined the issue "The Practice of Medicine by the Hospital" as well as the problems of supplying complete hospital service to rural areas and the role of government in educational and hospital service plans.

One of the pre-convention meetings presented outstanding pharmacists as faculty members in the 2nd annual Institute for Hospital Pharmacists sponsored by the Association. The Wisconsin Society of Hospital Pharmacists was in charge of the exhibit sponsored by the Division of Hospital Pharmacy of the A. PH. A. and the American Society of Hospital Pharmacists.

## MANUFACTURERS

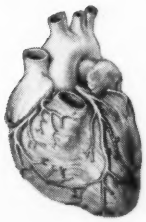
**Parke, Davis & Co.** announces plans for a new British plant at Hounslow, England. Chloromycetin will be produced for countries comprising the pound sterling areas. Dr. A. William Lescohier, president of the firm, said, "We decided to build the plant because we were determined that no country should be deprived of Chloromycetin as a result of the dollar shortage. The plant will serve the British Commonwealth, the British Colonies, the British Armed Services and other countries whose economy is closely linked with the pound sterling."

Dr. Lescohier explained that the British Ministry of Health had cooperated by granting priorities for the new building.

**Warner-Hudnut** dedicated its new West Coast headquarters at 2340 Easter Avenue, Los Angeles, June 26. The new plant, which cost $500,000, will house sales and staff offices and warehouse and shipping facilities. Eventually a manufacturing unit will be added. It is the latest structure to be completed in the Warner-Hudnut expansion plans. Elmer H. Bobst, Warner-Hudnut president, saluted the new plant and Los Angeles, "For intensive distribution, Los Angeles today is one of the key centers of the United States. We look upon our Los Angeles plant not as a branch of our Eastern establishment, but as an integral part of the community it serves."

The first industrial installation of an electron accelerator—popularly called an atom smasher—has just been completed in the research laboratories of **The Upjohn Company,** Kalamazoo, Mich. Because the high-energy radiations of the instrument can penetrate thick sections of steel, the Upjohn equipment is enclosed in five tons of iron bricks to protect personnel. Its potential usefulness in the sterilization of drugs led the Upjohn Company to undertake this tremendous and expensive installation. It is possible that the usefulness of high-speed electrons may go far beyond mere sterilization, perhaps increase antibiotic yields through mutation of

*(Continued on Page 452)*



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a new and promising attack on the problem of

**anginal pain**

'ESKEL'—an outstanding new coronary vasodilator—is a mixture of active principles, chiefly khellin, extracted from the Mediterranean plant, **Ammi visnaga.**

Exhaustive pharmacological studies with 'Eskel' have shown that it has at least 5 times the coronary dilating activity of aminophyllin . . . with an unusually prolonged action.

Clinical investigations by leading cardiologists have demonstrated that 'Eskel' gives marked relief to a high percentage of angina pectoris patients. (It is also reported to be of considerable value in chronic bronchial asthma.)

**You should anticipate an immediate demand for this welcome new drug. 40 mg. tablets of 'Eskel' are available now at your wholesaler in bottles of 50; list price, $29.16 doz.**

**For best retail profit, order at least 2/12 doz. bottles from your wholesaler TODAY.**

*Smith, Kline & French Laboratories, Philadelphia*

'Eskel' Trademark

**BRIEFLY NOTED** • • • • • • *from page 450*

antibiotic-producing molds. Upjohn's Research Division, however, has made it very plain that all this is still in the research stage.

Roland H. Noel, director of control at **Bristol Laboratories Inc.,** Syracuse, has been named a Fellow of the American Society for Quality Control and appointed chairman of the Society's Chemical-Technical Section. Mr. Noel is a member of the Combined Contact Committee of the American Pharmaceutical Manufacturers' Association and the American Drug Manufacturers' Association, and a member of the A. PH. A.

Additions have been made recently to the staff of the new Antibiotic Division of **Chas. Pfizer & Co., Inc.** Dr. Francis E. Martin, formerly in the Chemical Research Division of Ciba Pharmaceutical Products, Inc., will be director of medical service. Fred C. Sands, formerly with Hoffmann-La Roche, Inc., will be assistant sales manager.

Two promotions in the top scientific executive staff of the **Wm. S. Merrell Co.** have been announced. Dr. Robert S. Shelton, vice-president and director of the company and a member of Merrell's scientific staff since 1933, was appointed to the new post of Research Adviser to Top Management. Dr. Shelton's new duties involve over-all evaluation, planning and coordinating of product research and development. Dr. Harold W. Werner, associated with Merrell as head of the pharmacology department since 1943, was made director of scientific laboratories. In his new post, he will be responsible for the direction and operation of all Merrell Scientific Laboratories. Dr. Werner is a member of the A. PH. A.

**Schenley Laboratories** has arranged through officials of the American Legion National Rehabilitation Commission and Schenley Legion Post 1190 to give to the American Heart Association one billion units of penicillin for research in rheumatic fever.

## AT RANDOM

**Dr. and Mrs. E. N. Meuser,** who have been associated with missionary pharmaceutical work in West China since 1909, are retiring from the West China Union University. They are to leave for Canada as soon as travel from China is permitted. They may be addressed in care of the United Church of Canada, Mission Rooms, 299 Queen Street, W., Toronto, Ontario, Canada.

Oregon's 62nd annual Rose Show was not exactly the place to expect a pharmacist. But one was there—a winner! **Irwin L. Betzel,** of Eugene, won nine prizes with 13 entries from his 250 bush rose garden. One of the Betzel entries, the Peace rose, took grand sweepstakes honors with a score of 91 points—only 9 short of perfection.

Lynwood Leavitt, Norfolk, has been named secretary-treasurer of the **Virginia State Board of Pharmacy,** according to an announcement made by Howard G. Whitehead, board president. Mr. Leavitt succeeds A. L. I. Winne, who died in February after serving the board as chief administrator since 1919. Graduated from the Medical College of Virginia School of Pharmacy in 1941, Mr. Leavitt served throughout the war in the Navy and is now a Lieutenant in the Medical Service Corps, Naval Reserve.

More than a drugstore, **H. R. Horne & Sons** in Fayetteville is an institution. It is North Carolina's oldest drugstore and Fayetteville's oldest business establishment. Unchanging appearance of the 85-year-old Horne's has made it a landmark. Now the landmark is giving way to construction of a complete new modern building.

Shown for the first time at the British Industries Fair in New York, a new process for **printing on glass** ampules and containers attracted the attention of American pharmaceutical manufacturers. A special glass firing-in-ink is one part of the process developed by Rejafix, Ltd. of London.


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# A. Ph. A. Branches

## LOCAL BRANCHES

AT THE June meeting of the **City of Washington Branch,** Dr. John W. Cronin discussed "The National Hospital Survey and Construction Act and Its Effect upon the Community, the Citizen, and the Pharmacist." Dr. Cronin, Chief, Division of Hospital Facilities, U. S. Public Health Service, is particularly well qualified in the field of community health and hospital planning.

Changes in the list of officers of the new **Western Nebraska Branch** were made necessary when Treasurer Eldon Kriemer moved to Lincoln. George Lonie was elected to the office and a new membership committee chairman will be appointed to take Mr. Lonie's place. At the May meeting James Hayhurst, M.D., a urologist, gave an interesting talk on his field of medicine. Branch plans for the summer call for informal meetings and picnics—without 10-gallon hats, no doubt.

Newly elected officers of the **Northern New Jersey Branch** are: Jacob Eisen, president; Alexander Bell, Jr., vice-president; Michael Iannarone, secretary; Cyrus L. Cox, treasurer.

"Pharmacy and the United States Public Health Service" was the topic of the address given by George F. Archambault, chief of the pharmacy section of the U.S.P.H.S., at the **Baltimore Branch** May meeting.

## STUDENT BRANCHES

A RECORD of 37 years' service in one school was recognized when the **Alabama Polytechnic Institute School of Pharmacy Student Branch** joined with Rho Chi to honor the school's dean, Lynn Stanford Blake. "Dean Blake Day" was celebrated May 17.

"Swing your partner!" and the **University of Arizona Student Branch** swung right into the barn dance it sponsored to honor the pharmacy school's first graduates. Governor Dan E. Garvey, luncheon guest of the University of Arizona Student Branch, lauded the students who were entering "one of the noblest and most exacting professions."

As a part of the college centennial celebration, the **Cincinnati College of Pharmacy Student Branch** sponsored an open house with displays and exhibits showing 100 years of progress in the profession of pharmacy.

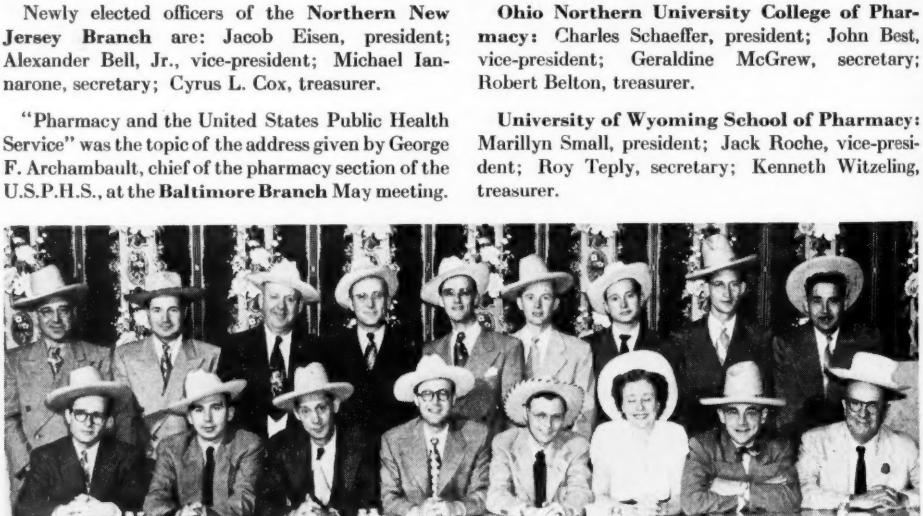
Election News! Officers have been installed for 1950–51 in many **Student Branches**——

**Rutgers University College of Pharmacy:** Philip A. Sachs, president; Bernard M. Gecker, vice-president; Rita Doctofsky, secretary; Samuel Jaffee, treasurer.

**University of Kansas City School of Pharmacy:** Harold (Jack) Magee, president; Fred Mahaffey, vice-president; Imogene Dreher, secretary; David Chun, treasurer.

**Ohio Northern University College of Pharmacy:** Charles Schaeffer, president; John Best, vice-president; Geraldine McGrew, secretary; Robert Belton, treasurer.

**University of Wyoming School of Pharmacy:** Marillyn Small, president; Jack Roche, vice-president; Roy Teply, secretary; Kenneth Witzeling, treasurer.



*Western Nebraska "ranch" Branch in 10-gallon hats: Dr. James Hayhurst, speaker; W. G. Lonie, treasurer; W. E. Lawrence, vice-president; Maurice Blazier, president; Glen G. Hoskinson, Jr., secretary; Ella Myers, Albert P. Hauke, Richard Glumn; (back row) Guy E. Stevens, L. B. Rogers, W. C. Colson, C. V. Kennedy, G. R. Myers, Jack W. Reece, Orville J. Peters, Martin J. Bakken, Virgil Boyd.*

# New A. Ph. A. Members

THE ASSOCIATION EXTENDS A CORDIAL WELCOME TO THE FOLLOWING MEN AND WOMEN WHO WERE ACCEPTED FOR ACTIVE MEMBERSHIP DURING THE MONTH PRECEDING PREPARATION OF THIS ISSUE.

### NEW LIFE MEMBERS

Patel, Babubhai N., Clarksville, Ark.
Smith, Dr. Austin, Chicago, Ill.

### ALABAMA

Landham, Thomas Jackson, Lincoln

### ARIZONA

Riddle, Harry R., Tucson
Simon, Louis J., Phoenix

### ARKANSAS

Walker, Dr. Fred A., Clarksville

### CALIFORNIA

Allison, Jay H., San Jose
Baker, Harry E., Jr., Monrovia
Buell, L. R., Fullerton
Chesbro, Wayne P., Berkeley
Epstein, Seymore L., Los Angeles
Muller, Catherine L., San Pedro
Otto, Mrs. Fern C., Los Angeles
Podhurst, Nathan, San Francisco
Yoon, Henry, Jr., Los Angeles

### CONNECTICUT

Feustel, William K., Norwalk

### DELAWARE

Coletta, Charles J., Wilmington

### DISTRICT OF COLUMBIA

Terry, Lewis S., Washington

### ILLINOIS

Austin, William L., Chicago
Bendry, Joseph A., Chicago
Broskuf, Maxwell, Chicago
Derman, Sigman, Chicago
King, Elmer G., Palos Hts.
Skye, Joseph F., East St. Louis

### INDIANA

Berry, Joe W., Seymour
Kovas, Dolores M., South Bend
Segall, Harry, Indianapolis
Sullivan, Mac L., Indianapolis
Zufall, Chalmers J., West Lafayette

### IOWA

Burleson, Harold H., Fort Dodge
Knight, Carl K., Council Bluffs

### LOUISIANA

LeRay, Harold B., DeRidder

### MARYLAND

Greenberg, Shirley G., Baltimore
Morris, Irving M., Baltimore
Wolfe, Morris, Baltimore

### MASSACHUSETTS

Scofield, Milton E., Melrose
Tura, Leon P., Kingston

### MICHIGAN

Morgan, Richard L., Kalamazoo
Parker, Muriel E., Ann Arbor
Rundman, Sven J., Kalamazoo
Sachs, Ronald A., Kalamazoo
Simon, Karl A., St. Joseph
Weiser, Harold D., Mancelona

### MINNESOTA

Berscheid, James B., Minneapolis
Dietz, Joseph L., Tracy
Sansby, J. D., St. Paul

### MISSOURI

Alberstat, Nathan G., St. Louis
Barry, Howard P., Jennings
Cunetto, Vincent J., St. Louis
Ellis, O. H., Clayton
Hearle, Stanley, St. Louis
Horne, George V., Rock Hill
Meyerson, Martin N., St. Louis
Moultrie, Forrest E., St. Louis
Mueller, John A., Affton
Reddish, George F., St. Louis
Roberts, Walter N., St. Louis
Ross, Edward J., St. Louis
Schroer, Martha, Webster Groves
Winkelmann, Aloys G., St. Louis

### NEBRASKA

Bursik, Jean R., Omaha
Burton, Thomas C., Omaha
Mahoney, Earl G., Omaha
Myers, Ella M., Gering
Navarra, Dominic V., Omaha
Prescher, Donald A., Omaha
Roettger, Hugh R., Imperial
Saner, John V., Omaha
Snodgrass, Milan C., Osceola

### NEW JERSEY

Ball, Arthur D., Rutherford
Blanck, Abraham, Newark
Cocco, Peter, Orange
Crawford, Mrs. Agnes T., Atlantic City
Dayharah, Teresa C., Teaneck
Gould, Herman A., Elizabeth
Kern, Donald H., Hammonton
Kouten, Joseph W., Woodbridge
La Forge, Raymond A., Orange
Meyers, Charles R., Westfield
Nixon, G. William, Alpine
Ordille, Anthony S., Egg Harbor City
Orleanski, Edmund B., Bayonne
Risner, Lewis, Merchantaville
Rosenberg, Abe, Passaic
Schreiber, Samuel C., Ventnor City
Shaw, George L., Fairlawn
Thorne, Elizabeth K., Camden
Tucker, Henry, Hoboken
Weintraub, Samuel, Westfield
Whitehead, Charles R., Orange
Williams, James H., Ridgewood
Wilson, Fred E., Ridgewood

### NEW MEXICO

Cloman, W. A., Carlsbad

### NEW YORK

Andrews, Lionel T., Flushing
Broadhead, Arthur D., Ithaca
Chapman, Walter G., Stapleton
Ells, Stanley L., Geneva
Fleszar, Jane C., Binghamton
Frost, Harry E., Buffalo
Harris, Hugh C., New York 11
Heeder, Caryl E., Rensselaer
Landis, Larry, New York
Loro, Joseph R., Schenectady
MacWatt, J Allan, Pearl River
Meisner, Milton L., Flushing
Monteith, Melvin E., Buffalo
Rimer, Louis, Bayside
Rowe, H. Sterling, New York
Savarese, Louis, New York
Schulman, Mandel, Bronx
Spaulding, Violet S., Albany
Timolat, James G., Jr., New York
Towers, Harry J., Forest Hills
Van Stone, T. B., New York

### NORTH CAROLINA

Caudle, Virginia, Concord
Sheffield, William J., Chapel Hill

### OHIO

Crow, Richard E., Middletown
Heckler, H. Grant, Mt. Vernon
Keyl, Milton J., Cincinnati
Levy, Elvera M., Cincinnati
May, L. A., Marietta
Neely, James S., Hamilton
Tenney, Robert E., Cincinnati

### OKLAHOMA

Cobb, J. C., Tishomingo
Lett, Robert F., Moore

### OREGON

David, Norman A., Portland
Smith, Cyril G., Portland

### PENNSYLVANIA

Cohen, Morris, Norristown
Connor, Edwin J., Kennett Square
Crossett, John, Jr., Worthington
Dereskevich, John A., Minersville
Edmundowicz, Alphonse, Nanticoke
Edwards, William M., Kingston
Goldblum, Norman P., Philadelphia
Goldsmith, Lee, Philadelphia
Gould, John, Emmaus
Handelsman, Eugene J., Belle Vernon
Herman, Samuel, Philadelphia
Kaczmarczyk, Michael, Mahonoy
Kuchemba, Stanley S., Pittston
Leisner, Joseph, Bethlehem
Mack, Harry, Philadelphia
Mayer, Harry O., Finleyville
Morse, John W., Union City
Neff, Harry, Philadelphia
Nenstiel, William H., Lancaster
Pahner, Wilfred S., Cincinnati
Pyle, C. B., Philadelphia
Schneiderwirth, Herman J., Jenkintown
Slomowitz, Samuel J., Swoyerville
Utsunomiyr, Rose S., Philadelphia

## NEW MEMBERS • • • • • • • *from page 455*

**SOUTH CAROLINA**
Kaiser, Horace M., Columbia

**TEXAS**
Harrell, William B., Jr., Houston
Sr. Mary Reginald Finlay, Beaumont

**UTAH**
Sister M. Rebecca Schmidt, Ogden

**VIRGINIA**
Skydanek, Bernard, Newport News

**WASHINGTON**
Brands, Allen J., Mercer Island
Hall, Mary P., Seattle.
Huffman, Elwood C., Coulee Dam.
Rains, Walter R., Everett.

**WEST VIRGINIA**
Hickman, John R., III. Princeton
Lawrence, William R., Huntington.
Thompson, Ronald E., Jr., Crab Orchard

**WISCONSIN**
Foye, William O., Madison
Gelb, Theodore P., Milwaukee
Johnson, J. Arthur, Whitehall
Reblitz, Lewis E., Fond Du Lac
Shaw, Harold W., New London
Soell, Mack G., La Crosse

**WYOMING**
Morgan, Frank J., Glenrock

**U. S. POSSESSIONS**
Gotay, Hilia J., Hato Rey, Puerto Rico

**FOREIGN**
Chung-Leung, Cheung, Causeway Bay, Hong Kong
Das, Durga Charan, West Bengal, India
Dhir, Mohan Lal, Bombay, India
Lachance, Andre, Quebec, Que., Canada
Shaw, Daile J., Sudbury, Ont., Canada
Sister Rose de Lima, Pusan, Korea

### Deceased Members

Alley, Lehman M., Birmingham, Ala., May 30, 1950
Barrett, Leslie B., New Haven, Conn., May 17, 1950
Fitz-Simon, Vincent J., Providence, R. I., April 11, 1950
Freiday, Don S., Bartlesville, Okla.
Griffith, Bates L., Kansas City, Mo.
Hay, Edward A. (a life member), Portland, Me., Feb. 17, 1950
Horlick, Alexander J. (a life member since 1904), Racine, Wis., June 7, 1950
Law, Frank F., West Collingswood, N. J., June 5, 1950
Lloyd, Kenneth W., Denver, Colo., Aug. 15, 1949
Napieralski, John A., Buffalo, N. Y., Oct. 10, 1949
Nash, Wm. B., Jr., Weymouth, Mass., Dec. 30, 1949
North, Herman H., Bloomfield, N. J., May 18, 1950
Novack, C. A., Minneapolis, Minn., May 10, 1950
Schultz, John J., Columbus, Wis.
Smith, Wheaton B., Toledo, Ohio, May 1, 1950
Thomure, Francis A., Olney, Ill., Apr. 4, 1950
Trimolat, Jas. G., New York, N. Y., Dec. 27, 1949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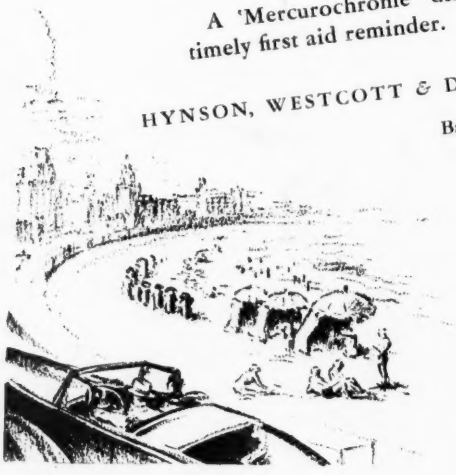
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